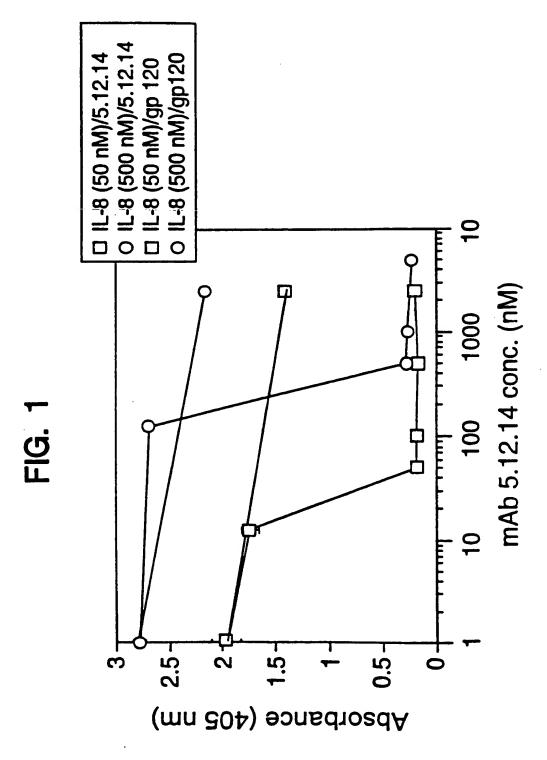
Hsei et al

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

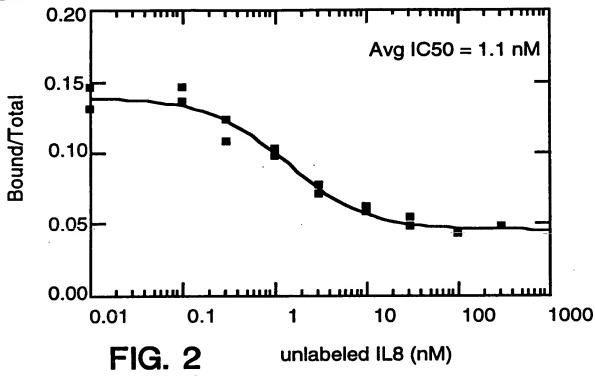


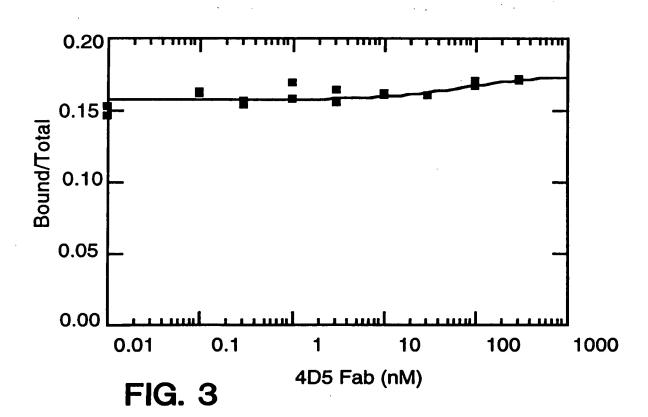


Appl. No.: 09/234,182

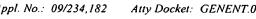
Atty Docket: GENENT.093A

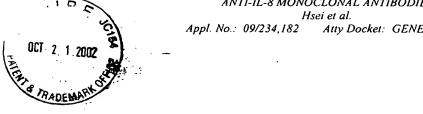


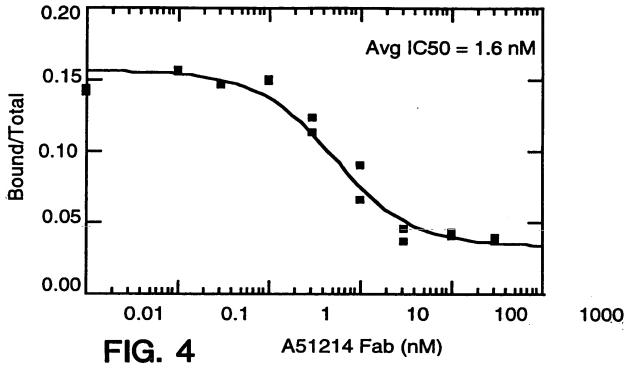


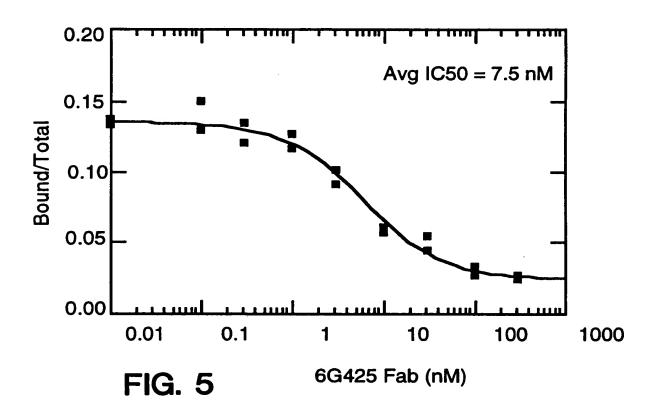


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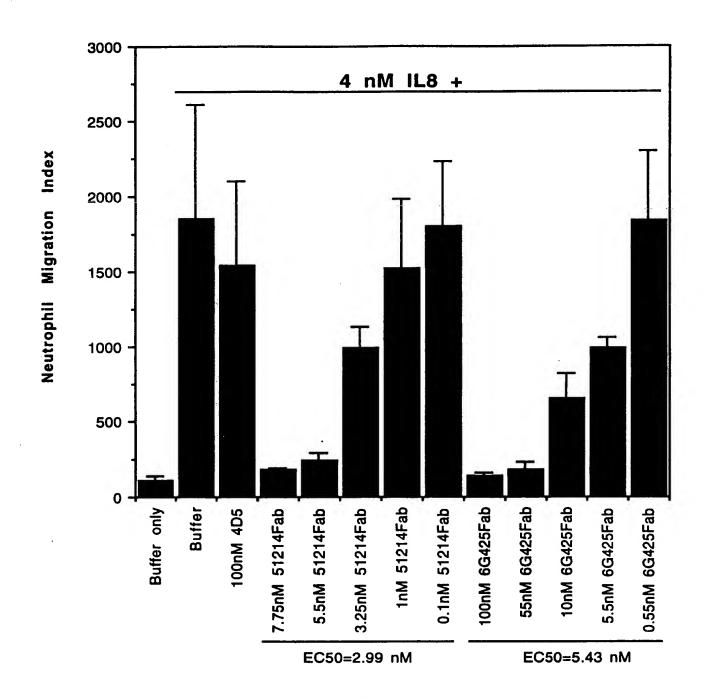


FIG. 6



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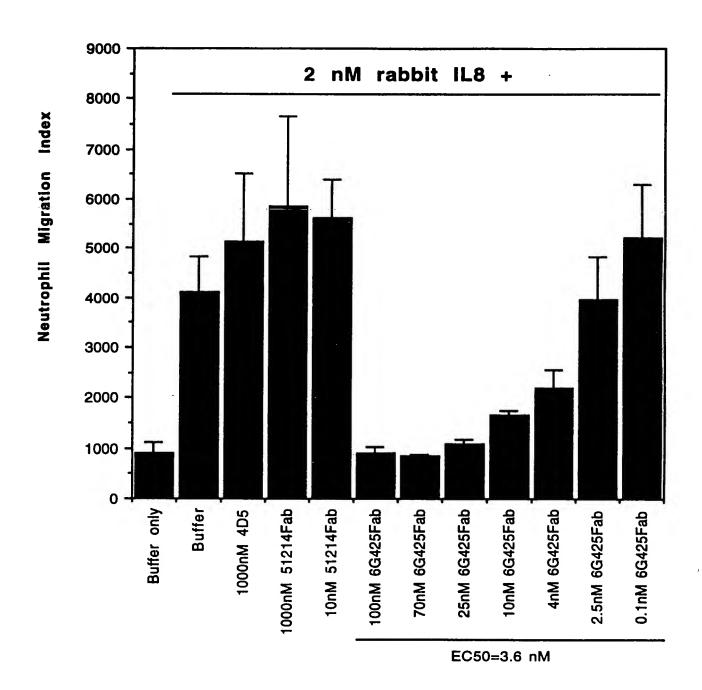
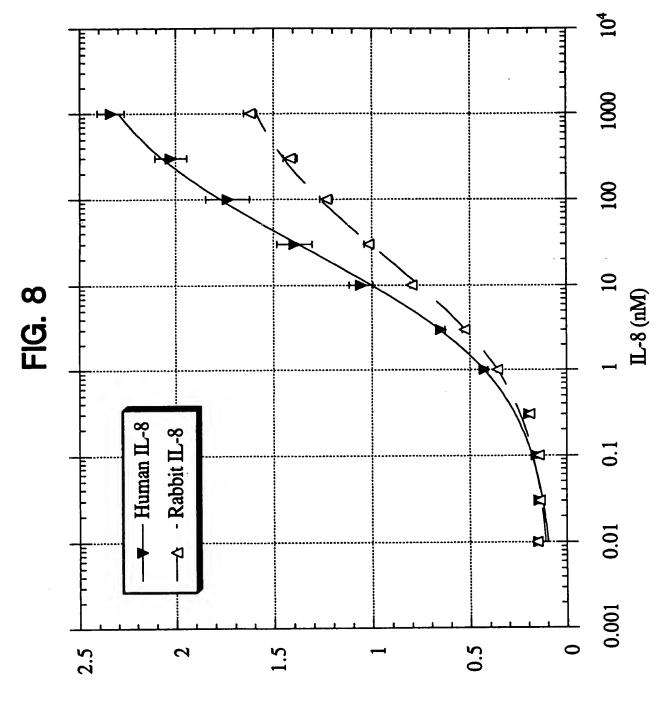


FIG. 7

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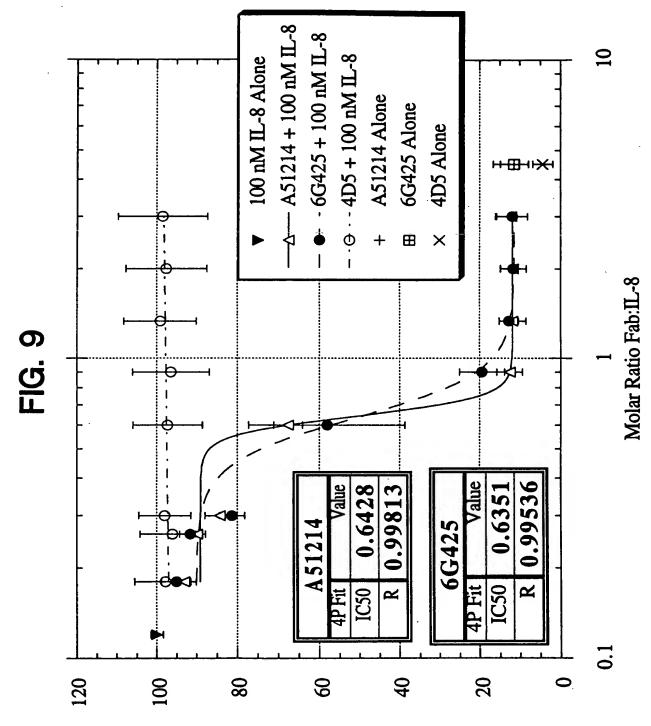


Absorbance (405 nm)

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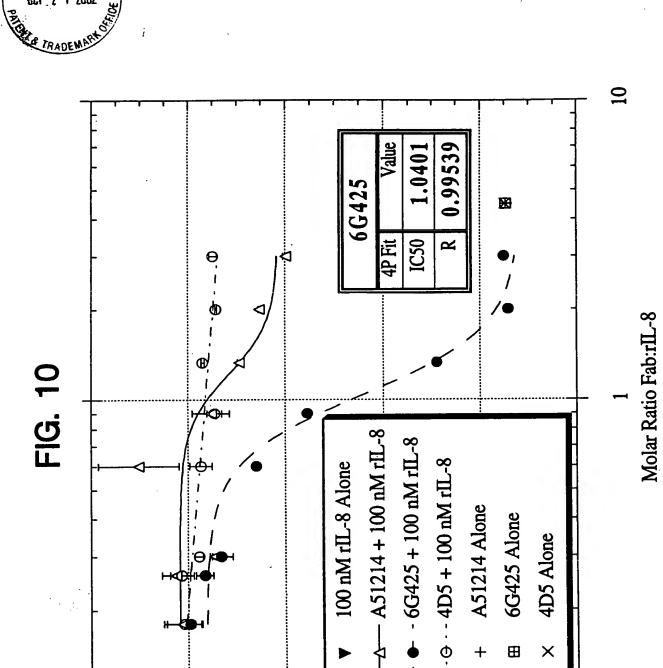




% IL-8-Stimulated Elastase Release

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES Hsei et al.

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Absorbance (405 nm)

9.0

0.8

0.4

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0.2

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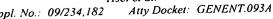
0

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES Hsei et al. Atty Docket: GENENT.093A Appl. No.: 09/234,182 OCT 2 1 2002 17 mg/mL TNBS n=5 iv anti-IL-8 FIG. 11B 17 mg/mL TNBS n=14 iv saline <u>|</u> Untreated 91 8 5 8 \$ pg/mg Tissue (mean±SEM) 17 mg/mL TNBS n=5 iv anti-IL-8 **MYELOPEROXIDASE** FIG. 11A 17 mg/mL TNBS n=14 iv saline Untreated 9 8 20 \$ 8 8 8 (M3S±nsem) etunim/dOm

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES Hsei et al. Atty Docket: GENENT.093A Appl. No.: 09/234,182 OCT 2 1 2002 17 mg/mL TNBS n=5 iv anti-IL-8 GROSS INFLAMMATION FIG. 11D 17 mg/ml TNBS n=14 iv saline Untreated 9 င္တ \$ ဗ္ဗ ୡ ė (GS±nsem) DUA 17 mg/mL TNBS n=5 iv anti-IL-8 **COLON WEIGHT** FIG. 11C 17 mg/mL TNBS n=14 iv saline Untreated Ą mg/cm/kg Body Weight mean±SD উ ই 33 8

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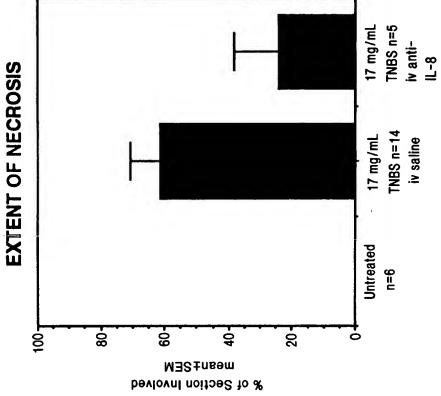
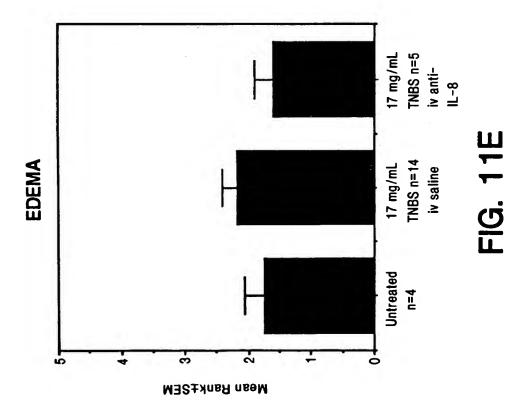


FIG. 11F



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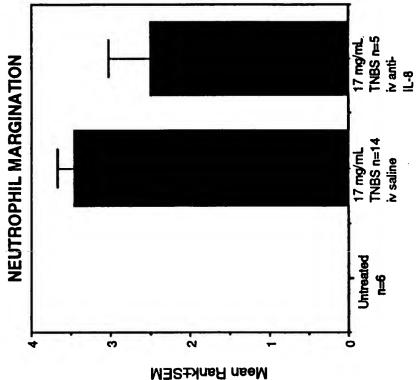
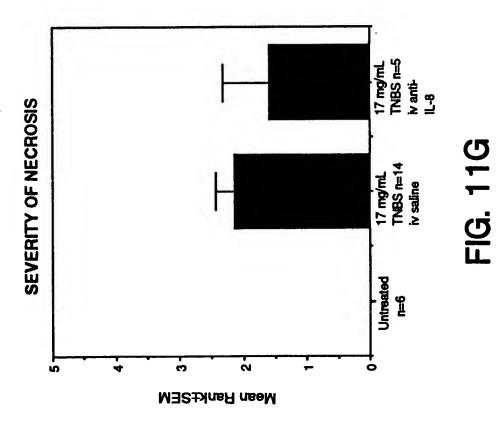
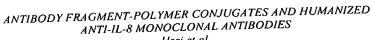


FIG. 11H

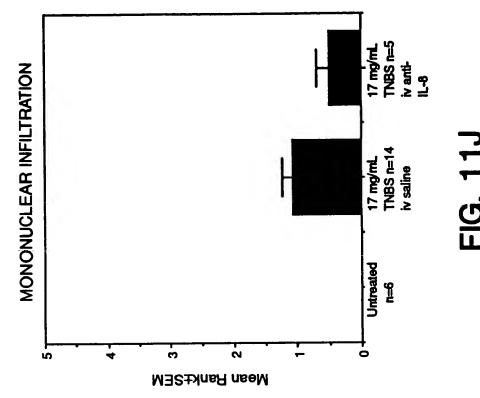


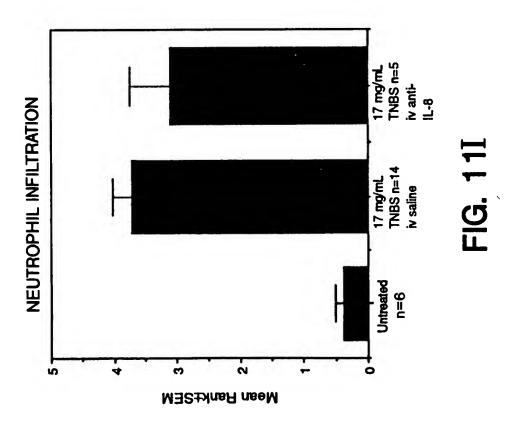


Hsei et al.

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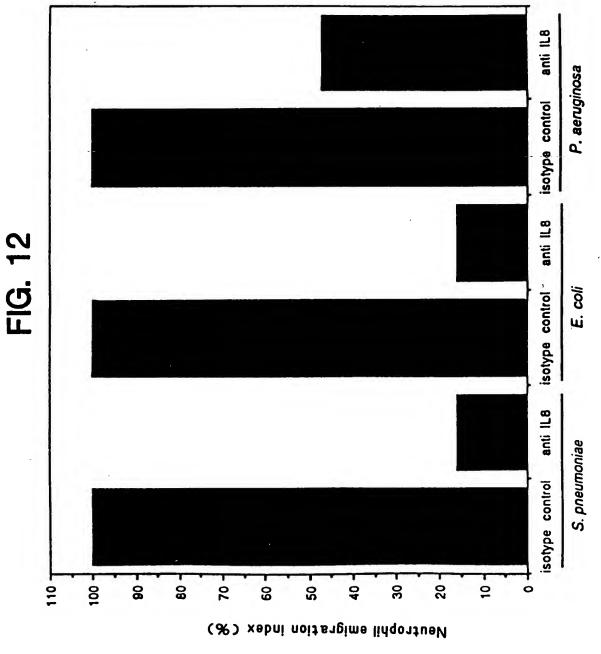






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Group (n=5 rabbits per group)



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Light Chain Primers:

MKLC-1, 22mer

FIG. 13

5' CAGTCCAACTGTTCAGGACGCC 3' (SEQ ID NO.1)

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3'(SEQ ID NO.2)

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3'(SEQ ID NO.3)

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3'(SEQ ID NO.4)

IGG2AC-2, 22mer

CACTGGCTCAGGGAAATAACCC 3 '(SEQ ID NO.5)

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3' (SEQ ID NO.6)



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Light chain forward primer

35 mer SL001A-2 3 ' (SEQ ID NO.7) (SEQ ID NO.8) (SEQ ID NO.9) 5' ACAAACGCGTACGCT GACATCGTCATGACCCAGTC

HA

3 '(SEQ ID NO.10)

37 mer SL001B

Light chain reverse primer

5' GCTCTTCGAATG GTGGGAAGATGGATACAGTTGGTGC



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(SEQ ID NO.14)

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Heavy chain forward primer

mer

39

SL002B

5' CGATGGCCCGG ATAGACCGATGGGCTGTTGTTTGGC 3' (SEQ ID NO.11)
T
C (SEQ ID NO.12)
G (SEQ ID NO.13)

H U A

Heavy chain reverse primer

39-MER SL002B 5' CGATGGGCCCGG ATAGACCGATGGGGCTGTTTTGGC

HAU

3 ' (SEQ ID NO.11) (SEQ ID NO.15) (SEQ ID NO.14) (SEQ ID NO.13)



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GTCCCAGTCG CAGGGTCAGC > 凶 GACATIGICA IGACACAGIC ICAAAAAIIC AIGICCACAI CAGIAGGAGA TACAGGTGTA GTCATCCTCT Ö > ഗ CTGTAACAGT ACTGTGTCAG AGTTTTTAAG × Ø >

ACAGAAACCA TGTCTTTGGT Ø CCTGGTATCA GGACCATAGT 3 GAATGTGGGT ACTAATGTAG CTTACACCCA TGATTACATC **K** * Ö GTCACCTGCA AGGCCAGTCA CAGTGGACGT TCCGGTCAGT 0 K ပ E > 61

CDR #1

AGTCCCTGAT TCAGGGACTA GATTTACTCG TCATCCTACC GGTACAGTGG CCATGICACC വ CTAAATGAGC AGTAGGATGG 召 * Н 121 GGGCAATCTC CTAAAGCACT GATTTCGTGA ď × CCCGTTAGAG ഗ Ø

CDR #2

ACACGTCAGA TGTGCAGTCT CGCTTCACAG GCAGTGGATC TGGGACAGAT TTCACTCTCA CCATGAGCCA ACCCTGTCTA AAGTGAGAGT GGTAGTCGGT ഗ Ы F. Ω E ტ CGTCACCTAG Ö ഗ GCGAAGTGTC

CAAGCCAGGA GTTCGGTCCT GAAGACTIGG CAGACTAITI CIGICAGCAA TAIBACAICI AICCICICAC ATATTGTAGA TAGGAGAGTG ы GACAGTCGTT Ø ပ GTCTGATAAA CTTCTGAACC Ω 241

CATCTTCCCA GTAGAAGGGT GGGACCAAGC TGGAGTTGAA ACGGGCTGAT GCTGCACCAC CAACTGTATC TGCCCGACTA CGACGTGGTG GTTGACATAG ۵ ø Ø Ø æ CCCTGGTTCG ACCTCAACTT Ц 回 G 301 101

BstBI

CCATTCGAA (SEQ ID NO.16) 361

(SEQ ID NO.17) GGTAAGCTT 回 Ŀ Q, 121

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61													CTCT GAGA	CC	TAA	GTA	TΑ	AGTO	ATC	
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FIG. 18

VL.front 31-MER

5 ' ACAA<u>ACGCGT</u>ACGCT<u>GATATC</u>GTCATGACAG 3 ' (SEQ ID NO.20)

VL.rear 31-MER

5' GCAGCATCAGCTCTTCGAAGCTCCAGCTTGG 3'(SEQ ID NO.21)

VH.front.SPE 21-MER

5 ' CCACTAGTACGCAAGTTCACG 3 ' (SEQ ID NO.22)

VH.rear 33-MER

5 ' GATGGGCCCTTGGTGGAGGCTGCAGAGACAGTG 3 ' (SEQ ID NO.23)

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61					ATAT															
-3	A				TATA I	GCA V		T	Q	S	Q Q			M	S	T	S	V		
121					TCAC															
	TC	CCA	GTC	GC	AGTG	GAC														
18	R	V	S	V	T	С	K	A	<u>s</u>	0	<u>N</u> _	<u>V</u>	<u>_G</u> _	<u>T</u>	N	V	A	W	Y	Q
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181					GGCA															
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241					GCTT															
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58	V	P	D	R	F	T	G	S	G	S	G	T	D	F	Т	L	T	I	S	Н
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421					CTGA'															
118					D															
404																				
481					CCAG.															
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										-								-		
541					AGAG'															
150					TCTC												GTC S			
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601	ACC	CT	GAC	GC	TGAG	CAA	AGC	AGA	CTA	CGAG	AA	ACAC	CAA	AG	TCTA	CGC	CTG	CGA	AGTC	ACC
	TGO	GA(CTG	CG	ACTC				GAT	GCTC	TT	rgty	STT	ľC	AGAT	GCG	GAC	GCT'	rcag	TGG
178	T	L	T	L	S	K	A	D	Y	E	K	H	K	V	Y	A	C	E	V	T
661	CA:	rca(GG	CC	TGAG	CTC	GCC	CGT	CAC	AAAG	AGO	TTT	CAAC	CA	GGGG	AGA	GTG			
	GT	AGTY	CCC	GG	ACTC	GAG	CGG	GCA	GTG'	TTTC	TCC	SAAC	3TTC	ЗT	CCCC	TCT	CAC			
198	H	Q	G	L	S	S	P	V	T	K	S	F	N	R	G	E	C (S	SEQ I	DN	O.25)
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1	ATGAAA																
	TACTTT															ATG! T	
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61	GCGTAC																
-3	CGCATGO			CGTCG. O L		ACCT E	CAGA S	G			GA L		CGG P		ACC.	TCC(G	CAGG S
		_			-				_	-		•	_	_	_		
121	CTGAAAC																
18	L K I		_	A A			F						G	M	S	W	V
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									C	DR	#1						
181	CGCCAGA	ACTC	CAGG	CAAGA	G CC	TGGA	GTTG	GT	CGC	AAC	CA	TTAA	TAA	AAT	TGG	TGA!	TAGC
	GCGGTCT	rgag	GTCC	GTTET	e GG/	ACCT	CAAC	CA	GCG'	TTG	GT	AATT	ATT.	ATT	ACC	ACT	ATCG
38	R Q 7	r P	G	K S	L	E	L	V	A	T	I	N	N	<u>N</u> _	_G_	D	S
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241	ACCTATT																
	TGGATA	ATAG	GTCT														
58		Y P	D *	S V	K *	G	R	F	T	I	S	R	D	N	A	K	N.
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301	ACCCTGT TGGGACA																
78	T L N		O	M S		L		S		D	T	A		F	Y		A
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361	AGAGCCC TCTCGGC																
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				CDR	‡3												
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421	GTCTCTC																
118	CAGAGAC V S A	A A	GGAG	T K	r CCC	JGGG P	S	V	GAA F	eGG P	L	ACCG	P	S	S	K	S
481	ACCTCTC																
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FIG. 20A



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> 661 ACCCAGACCT ACATCTGCAA CGTGAATCAC AAGCCCAGCA ACACCAAGGT GGACAAGAAA CCTGTTCTTT Treggeregr reregrices TGGGTCTGGA TGTAGACGTT GCACTTAGTG

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(SEQ ID N0.26) 721

(SEQ ID NO.27) GTTGAGCCCA AATCTTGTGA CAAAACTCAC ACATGA CAACTCGGGT TTAGAACACT GTTTTGAGTG TGTACT V E P K S C D K T H T O T H Ŋ 闽 > 218

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# ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

Light Chain Primers:

MKLC-1, 22mer

5' CAGTCCAACTGTTCAGGACGCC 3' (SEQ ID NO.1)

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3' (SEQ ID NO.2)

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3'(SEQ ID NO.3)

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3' (SEQ ID NO.4)

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3' (SEQ ID NO.5)

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3' (SEQ ID NO.6)

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Light chain forward primer

36-MER 6G4.light.Nsi 3 ' (SEQ ID NO.28) (SEQ ID NO.29) (SEQ ID NO.30) 5' CCAATGCATACGCT GAC ATC GTG ATG ACC CAG ACC CC
T T T T A A A A

Light chain reverse primer

35-MER 6G4.light.Mun 5' AGA TGT CAA TTG CTC ACT GGA TGG TGG GAA GAT GG 3' (SEQ ID NO.31)

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Heavy chain forward primer

6G4.heavy.Mlu 32-MER

3 · (SEQ ID NO.32) (SEQ ID NO.33) 5' CAAACGCGTACGCT GAG ATC CAG CTG CAG CAG
T C

Heavy chain reverse primer

39-MER

SL002B

3 ' (SEQ ID NO.11) (SEQ ID NO.15) (SEQ ID NO.14) (SEQ ID NO.13) 5' CGATGGCCCGG ATAGACCGATGGGGCTGTTTTTGGC E A U

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### ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

70 G ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGGAGAT C TATAGCACTA CTGTGTCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA D I V M T Q T P L S L PVS 121 CAGGCCTCCA TCTCTTGCAG ATCTAGTCAG AGCCTTGTAC ACGGTATTGG AAACACCTAT GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA 18 Q A S I S C R S S Q SLVHGI G_ N ☆ * A * * * CDR #1 181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC AATGTAACCA TGGACGTCTT CGGTCCGGTC AGAGGTTTCG AGGACTAGAT GTTTCAAAGG 38 L H W Y L Q K P G Q SPKL LI K V S **CDR #2** 241 AACCGATTTT CTGGGGTCCC AGACAGGTTC AGTGGCAGTG GATCAGGGAC AGATTTCACA TTGGCTAAAA GACCCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT G V P D R F S G S G 58 N R F S SGT 301 CTCAGGATCA GCAGAGTGGA GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT 78 L R I S R V E A E D LGLY F C S Q S TCDR #3 361 CATGTTCCGC TCACGTTCGG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGATGCTGCA GTACAAGGCG AGTGCAAGCC ACGACCCTGG TTCGACCTCG ACTTTGCCCG ACTACGACGT AGTKLEL K R A D A A TFG 98 <u>H V P L</u> MunI 421 CCAACTGTAT CCATCTTCCC ACCATCCAGT GAGCAATTGA (SEQ ID NO.34) GGTTGACATA GGTAGAAGGG TGGTAGGTCA CTCGTTAACT P S S E Q L K (SEQ ID NO.35) 118 P T V S I F P

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# ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

70	G	AGA	TT	CAG	CT (	GCAG	CAGI	CT C	GAC	CTGA	.GC	TGA	TG	AAG	CC 7	rgg	GG	TT	CA		
	C	TCT	AA	GTC(	GA (	CGTC	GTCA	GA (	CTC	GACT	СG	ACT	'AC	rtc	GG A	ACCO	CCC	AAS	GT		
1	E	Ι	(	2	L	Q	Q S	C	3 I	E	L	M	1 1	K	P	G	A	S			
121	GI	GAA	GA'	ГАТ	CCI	IGCA	AGGC	ጥጥር	TGC	TATE	ידי	ייים:	YCA(	TTA	GCC	יאכיי	ra <i>c</i>	יעמי	GCA	CTC	ĊĊŦĊ
										AATA											
18		K		s			A			Y							·	M	Н	W	V
														*	1	-	r	*	*		
													CI	OR	#1						
1 2 1	ממ	CCA	CAC	יייי	አጥረ	מ מ בייב	አርአር	CCT	יחרי ז	GTGG	አብ	TUTTO C	יריתיז	እ <i>ነ</i> ፖን አ	mm	י איתער		v	<b>~</b> n-n	moc	תית איתו
, 101										CACC											
3.8		0		DD.		K		L	E E	W	I	G G	.GA. Y	I				S	N	G	E
50		V	3	**		, K		ы	E	VV		G	±	*		_	-	<u>.                                    </u>		<u>.</u>	E.
																CDF	. #	2	-	-	-
																	` "	_			
241	AC	TAC	TTA	CA	ACC	AGA	TTAA	CAA	GGG	CAAG	GC	CAC	'ATI	'GA	СТС	TAC	AC	AC	ATC	TTC	CAGC
										GTTC											
58		${f T}$	Y	N	Ç		F	K	G	K	A		L	$\mathbf{T}$	V			$\mathbf{T}^{-}$	S	S	S
	*	*	*	*	*	*	*	*	*												
301	AC	AGC	ממח	CG	ጥርር	ים דע מי	ፐርልር	CAG	ירריז	GACA	тC	מבישי	ጥር እ	·ርሞ	CTC	יראכ	<u>ነ</u> ጥር	יתי א	etretretre	ריזיכי	ጥርርእ
										CTGT											
78				v		L		S	L	T	S	D	D	S	A			Y	F		A
, ,	•	••	••	•	•		5	5		•	5	D		3		. •	'	•	F	C	Α
361	AG	AGG	GGA	CT	ATA	GAT	ACAA	CGG	CGA	CTGG	TT	TTT	CGA	TG	TCT	'GGG	GC	GC	AGG	GAC	CACG
	TC	TCC	CCI	'GA	TAT	'CTA'	rgtt	GCC	GCT	GACC	AA	AAA	GCI	'AC	AGA	CCC	CG	CG	TCC	CTG	GTG <i>C</i>
98	R	G	<u>D</u>	_Y	R	Y	N	G	D	W	F	F	D	V	W	G	}	A	G	T	יו
		*	*	*	*	*	*	*	*	*	*	*	*	*							
						CI	OR #3	3													
	В	stE:	ΙΙ														Αp	aI			
421	GT	'CAC	CGT	'CT	CCT	CCG	CCAA	AAC	CGA	CAGC	CC	CAT	CGG	TC	TAT	CCG	GG	CC			
	CA	GTG	<i>3</i> CA	GA	GGA	GGC	<b>GAT</b>	TTG	GCT	GTCG	GG	GTA	GCC	AG	ATA	.GG <i>C</i>	'CC	'GG			
118	V	T	V	S	S	Α	K	T	D	S	P	I	G	L	S	G		P			
471		TC AG	(SI	EQ 1	D N	O.36	)														
135			(SI	EO I	ID N	iO.37	1														
	_	-	(0)	-V		· • · • ·	,														



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5' CTTGGTGGAGGCGGAGGAGACG 3' (SEQ ID NO.38)

Mutagenesis Primer for 6G425VL

DS/VF 38MER

5' GAAACGGGCTGTTGCTGCACCAACTGTATTCATCTTCC 3'(SEQ ID NO.39)

SYN.BstEII 31 MER

5' GTCACCGTCT CCTCCGCCTC CACCAAGGGC C 3' (SEQ ID NO.40)

SYN.Apa 22 MER

5' CTTGGTGGAGGCGGAGGAGACG 3' (SEQ ID NO.38)

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1			TCTTCTTGCA AGAAGAACGT			
-23	M K K N	•	L L A	S M F V		A T N
61			GACACAGACA CTGTGTCTGT			
-3	AYAD		T Q T	P L S L	P V S	L G D
121			ATCTAGTCAG TAGATCAGTC			
18	Q A S I		S S O	SLVH	G I G	N T X
		*	* * *	CDR #1	* * *	* * *
181			GCCAGGCCAG			
38		L O K	CGGTCCGGTC P G Q	AGAGGTTTCG S P K L	AGGACTAGAT L I Y	
30	* *	гук	P G Q	2 P K L	пті	K V S
						CDR #2
241			AGACAGGTTC TCTGTCCAAG			
58		G V P	D R F	S G S G	SGT	D F T
	* * * *					
301			GGCTGAGGAT CCGACTCCTA		₩. \	
78	L R I S		A E D	L G L Y	F C S	O S T
, ,					*	* * *
						DR #3
361			TGCTGGGACC ACGACCCTGG			
9,8	H V P L	T F G	ACGACCCIGG	K L E L	K R A	V A A
	* * * *	*				• •• ••
421	ССХХСТСТАТ					
110			ACCATCCAGT			
	GGTTGACATA	AGTAGAAGGG	TGGTAGGTCA	CTCGTTAACT	TTAGACCTTG	ACGGAGACAA
	GGTTGACATA P T V F	AGTAGAAGGG I F P	TGGTAGGTCA P S S	CTCGTTAACT E Q L K	TTAGACCTTG S G T	ACGGAGACAA A S V
	GGTTGACATA P T V F GTGTGCCTGC	AGTAGAAGGG I F P TGAATAACTT	TGGTAGGTCA P S S  CTATCCCAGA	$ \begin{array}{cccc} \mathbf{CTCGTTAACT} \\ \mathbf{E} & \mathbf{Q} & \mathbf{L} & \mathbf{K} \\ \\ \mathbf{GAGGCCAAAG} \end{array} $	TTAGACCTTG S G T TACAGTGGAA	ACGGAGACAA A S V GGTGGATAAC
481	GGTTGACATA P T V F GTGTGCCTGC CACACGGACG	AGTAGAAGGG I F P TGAATAACTT ACTTATTGAA	TGGTAGGTCA P S S	$ \begin{array}{cccc} \mathbf{CTCGTTAACT} \\ E & Q & L & K \\ \\ \mathbf{GAGGCCAAAG} \\ \mathbf{CTCCGGTTTC} \end{array} $	TTAGACCTTG S G T  TACAGTGGAA ATGTCACCTT	ACGGAGACAA A S V GGTGGATAAC CCACCTATTG
481 138	GGTTGACATA P T V F GTGTGCCTGC CACACGGACG V C L L	AGTAGAAGGG I F P TGAATAACTT ACTTATTGAA N N F	TGGTAGGTCA P S S  CTATCCCAGA GATAGGGTCT Y P R	CTCGTTAACT E Q L K GAGGCCAAAG CTCCGGTTTC E A K V	TTAGACCTTG S G T  TACAGTGGAA ATGTCACCTT Q W K	ACGGAGACAA A S V GGTGGATAAC CCACCTATTG V D N
481 138	GGTTGACATA P T V F GTGTGCCTGC CACACGGACG V C L L GCCCTCCAAT	AGTAGAAGGG I F P  TGAATAACTT ACTTATTGAA N N F  CGGGTAACTC	TGGTAGGTCA P S S  CTATCCCAGA GATAGGGTCT Y P R  CCAGGAGAGT	CTCGTTAACT $E$ $Q$ $L$ $K$ GAGGCCAAAG CTCCGGTTTC $E$ $A$ $K$ $V$ GTCACAGAGC	TTAGACCTTG S G T  TACAGTGGAA ATGTCACCTT Q W K  AGGACAGCAA	ACGGAGACAA A S V  GGTGGATAAC CCACCTATTG V D N  GGACAGCACC
481 138 541	GGTTGACATA P T V F  GTGTGCCTGC CACACGGACG V C L L  GCCCTCCAAT CGGGAGGTTA	AGTAGAAGGG I F P  TGAATAACTT ACTTATTGAA N N F  CGGGTAACTC GCCCATTGAG	TGGTAGGTCA P S S  CTATCCCAGA GATAGGGTCT Y P R	CTCGTTAACT $E$ $Q$ $L$ $K$ GAGGCCAAAG CTCCGGTTTC $E$ $A$ $K$ $V$ GTCACAGAGC CAGTGTCTCG	TTAGACCTTG S G T  TACAGTGGAA ATGTCACCTT Q W K  AGGACAGCAA TCCTGTCGTT	ACGGAGACAA A S V  GGTGGATAAC CCACCTATTG V D N  GGACAGCACC CCTGTCGTGG
481 138 541 158	GGTTGACATA P T V F  GTGTGCCTGC CACACGGACG V C L L  GCCCTCCAAT CGGGAGGTTA A L Q S  TACAGCCTCA	AGTAGAAGGG I F P  TGAATAACTT ACTTATTGAA N N F  CGGGTAACTC GCCCATTGAG G N S  GCAGCACCCT	TGGTAGGTCA P S S  CTATCCCAGA GATAGGGTCT Y P R  CCAGGAGAGT GGTCCTCTCA Q E S  GACGCTGAGC	CTCGTTAACT $E$ $Q$ $L$ $K$ GAGGCCAAAG CTCCGGTTTC $E$ $A$ $K$ $V$ GTCACAGAGC CAGTGTCTCG $V$ $T$ $E$ $Q$ AAAGCAGACT	TTAGACCTTG S G T  TACAGTGGAA ATGTCACCTT Q W K  AGGACAGCAA TCCTGTCGTT D S K  ACGAGAAACA	ACGGAGACAA A S V  GGTGGATAAC CCACCTATTG V D N  GGACAGCACC CCTGTCGTGG D S T  CAAAGTCTAC
481 138 541 158 601	GGTTGACATA P T V F  GTGTGCCTGC CACACGGACG V C L L  GCCCTCCAAT CGGGAGGTTA A L Q S  TACAGCCTCA ATGTCGGAGT	AGTAGAAGGG I F P  TGAATAACTT ACTTATTGAA N N F  CGGGTAACTC GCCCATTGAG G N S  GCAGCACCCT CGTCGTGGGA	TGGTAGGTCA P S S  CTATCCCAGA GATAGGGTCT Y P R  CCAGGAGAGT GGTCCTCTCA Q E S	CTCGTTAACT $E$ $Q$ $L$ $K$ GAGGCCAAAG CTCCGGTTTC $E$ $A$ $K$ $V$ GTCACAGAGC CAGTGTCTCG $V$ $T$ $E$ $Q$ AAAGCAGACT TTTCGTCTGA	TTAGACCTTG S G T  TACAGTGGAA ATGTCACCTT Q W K  AGGACAGCAA TCCTGTCGTT D S K  ACGAGAAACA TGCTCTTTGT	ACGGAGACAA A S V  GGTGGATAAC CCACCTATTG V D N  GGACAGCACC CCTGTCGTGG D S T  CAAAGTCTAC GTTTCAGATG



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661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GTTGTCCCCT CCCGGACTCG AGCGGGCAGT GTTTCTCGAA CGGACGCTTC AGTGGGTAGT

Ŋ ტ 回

198

(SEQ ID NO.41) 721 GAGTGTTAA CTCACAATT

(SEQ ID NO.42) 0 U (a) 218

# FIG. 27B

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# ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES Hsei et al.

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1					ATAT TATA															
-23															F			A		
61					AGAT TCTA															
-3	A									S				-	M					
121					CCTG															
18	V					K				<u> Y</u>						Y *	M	H *		
													CD	R	<b>‡1</b>					
181					ATGG															
20					TACC															
30	V	Q	5	п	G	r	5	П	E	W	Т	G	Y	I	D *	<u> </u>	<u>\$</u>	<u>N</u> _	-Ĝ	E
													и	u		DR		H	w	н
241					ACCA TGGT															
58	T		Y	N	0	K	F	K							V			S		S
	#	*	<u>-</u>	#	*	#	±	#	*	•		•	_	•	•		•	J		J
301					TGCA ACGT															
70					ACGT:										GACG A					
361					ATAG.															
0.0					TATC															
98	R	G #	<u>υ</u>	<u> </u>	R_	<u> </u>		_G ≠	_υ	- <u>₩</u>	<u> </u>	<u>.F.</u>	_D	v	W	G	A	G	T	T
		-	-	-	-		R #3		•	•	•	•		*						
421	GTC	CACC	CGTC	T	CCTC	CGC	CTC	CAC	CAAC	GGC	CCI	ATC	GGT(	CT	TCCC	CCT	GGC	ACC	CTCC	CTCC
118					S				K						AGGG P					
110	•	•		٥	J	A	5	1	Λ	G	F	.5	V	r	P	Ъ	A	P	3	S
481					CTGG(															
138						G									K			F		
541	CCG	GTC	ACC	G G	TGTC	GTG	GAA	CTC	AGGC	CGCC	CTC	GAC	CAGO	CG	GCGT	GCA	CAC	СТТС	CCC	GCT
	GGC	CAC	TGC	C	ACAG	CAC	CTT	GAG'	rcco	CGG	GAC	CTGC	3TC(	ЗC	CGCA	CGT	GTG	GAAC	GGC	CGA
158					S				G		L		S			H			P	
601	GTC	CTA	CAC	T	CCTC	AGG/	ACT	CTAC	CTCC	CTC	AGO	CAGO	CGT	<b>3</b> G	TGAC	CGT	GCC	CTCC	CAGO	CAGC
178	V	GA'I T.	GTC	.A C	GGAG'		ľGA <i>L</i>		SAGG S			TCC S								
_,,	•		¥	J	ت	J	ப			چ ت	-	_	•	V	T	V	ע	S	S	S

FIG. 28A



Hsei et al.

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TIGGGCACCC AGACCTACAT CIGCAACGIG AATCACAAGC CCAGGAACAC CAAGGIGGAC GGTCGTTGTG GTTCCACCTG TTAGTGTTCG GACGTTGCAC AACCCGTGGG TCTGGATGTA 661

TTCTTTCAAC TCGGGTTTAG AACACTGTTT TGAGTGTGTA CT

(SEQ ID NO.44)

(SEQ ID NO.43)

721 AAGAAAGTTG AGCCCAAATC TTGTGACAAA ACTCACACAT GA

T Y

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198

218

FIG. 28B



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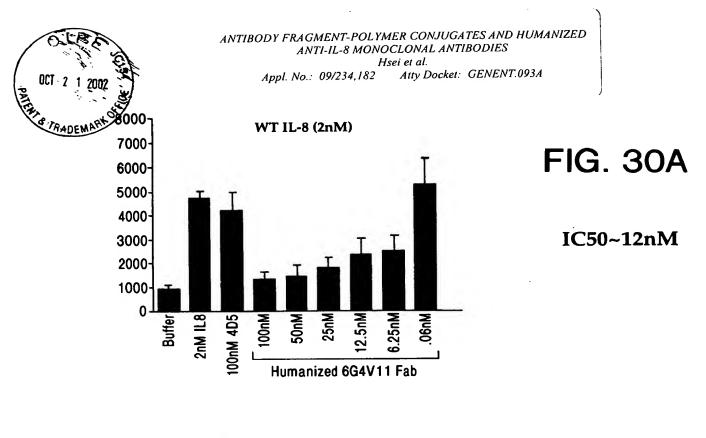
#### Variable Light Chain Domain

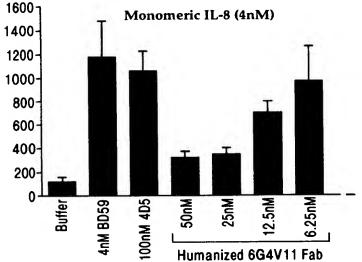
	10 20 abcde 30 40
6G425	DIVMTQTPLSLPVSLGDQASISCRSSQSLVHGIGNTYLHWYLQKPGQSPKLLIY
F(ab)-1	DIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTYLHWYQQKPGKAPKLLIY
humĸI	DIQMTQSPSSLSASVGDRVTITCRASKTISKYLAWYQQKPGKAPKLLIY
	==========
	******
	L1
	50 60 70 80 90 100
6G425	YKVSNRFSGVPDRFSDSGSGTDFTLRISRVEAEDLGLYFCSQSTHVPLTFGAGTKLELKR (SEQ ID NO.45)
	* * * * * * * * * * * * * * * * * * * *
F(ab)-1	YKVSNRFSGVPSRFSGSGSGTDFTLT1SSLQPEDFATYYCSQSTHVPLTFGQGTKVEIKR (SEQ ID NO.46)
	88 888
humĸI	YSGSTLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQHNEYPLTFGQGTKVEIKR (SEQ ID NO.47)
	===
	******
	L2 L3

#### Variable Heavy Chain Domain

	10 20 30 40														
6G425	EIQLQQSGPELMKPGASVKISCKASGYSFSSHYMHWVKQSHGKSLEWI														
F(ab)-1	EVQLVESGGGLVQPGGSLRLSCAASGYSFSSHYMHWVRQAPGKGLEWV														
	8 88 8 8														
humIII	EVQLVESGGGLVQPGGSLRLSCAASGFSFTGHWMMWVRQAPGKGLEWV														
	======														
	+++++														
	H1														
	50 a 70 80 abc 90 100 110														
6G425	GYIDPSNGETTYNQKFKGKATLTVDTSSSTANVHLSSLTSDDSAVYFCAARGDYRYNGDWFFDVWGAGT (SEO ID NO.48)														
F(ab)-1	GYIDPSNGETTYNQKFKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAARGDYRYNGDWFFDVWGQGT (SEO ID NO.49)														
humIII	GMIHPSDSETRYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAARGIYFY-GTTYFDYWGQGT (SEQ ID NO.50)														
	====														
	********														
	н2														

FIG. 29





**FIG. 30B** 

IC50~15nM

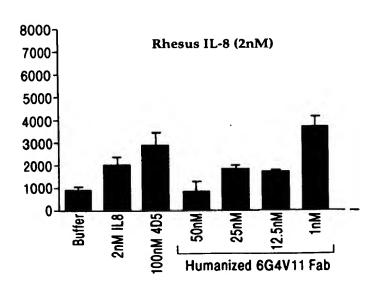


FIG. 30C

IC50~22nM

nsei 4ppl. No.: -09/234,182

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Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Light Chaim

ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG HVPLTFGOGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQST MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTY EC (SEQ ID NO.51) Amino Acid Sequence of the humanized anti-IL-8 6G4:2.5V11 Heavy Chain

WVRQAPGKGLEWVGYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT@TYICNVNHKPSNTK MKKNIAFLLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH VDKKVEPKSCDKTHT (SEQ ID NO.52) Amino Acid Sequence of the peptide linker and M13 Phage Coat (gene-III)

SGGGSGSGDFDYEKMANANKGAMTENADENALOSDAKGKLDSVATDYGAAIDGFIGDVS **GLANGNGATGDFAGSSNSQMAQVGDGDNSPLMNNFRQYLPSLPQSVECRPFVFSAGKPY** EFSIDCDKINLFRGVFAFLLYVATFMYVFSTFANILRNKES (SEQ ID NO.53)

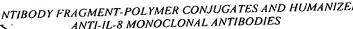
FIG. 31A

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ر نوم	ATGAAA																	
DEMARK	ATGAAA	AAGA	ATAT	CGCAT	ľΤ	TCT'	TCT'	TGCA	TC	ТАТ	GTT	CG	тттт	ттс	тат	TGC	TAC.	AAAC
	TACTTI																	
-23	M K	K N	I	A I	7	L	L	A	S	M	F	V	F	S	I	A	T	N
<i>C</i> 1	COAMAC	20000	<b>3</b> M 3 M	00101		<b>C1</b> C	~~~	omoo.	~~	<b>~</b> ~ ~	c.m.c		mama					
91	GCATAC																	
-3	A Y			0 1				S		S				A			G	
				_			_				_		_		_	•	_	_
121	AGGGTC																	
10	TCCCAG																	
10	R V	T I	Т	C F	(	5	5	Q	5	L	٧	н	G	I	G	N	T	Y
181	TTACAC	TGGT	ATCA	ACAG!	LΑ	ACC	AGG	AAAA	GC	TCC	GAA	AC	TACT	GAT	TTA	CAA	AGT	ATCC
	AATGTG	ACCA	TAGT	TGTCT	Т	TGG	rcc'	TTTT [*]	CG.	AGG	СТТ	ΤG	ATGA	CTA	ААТ	GTT	rca'	<b>FAGG</b>
38	L H	W Y	Q	Q I	7	P	G	K	A	P	K	L	L	I	Y	K	V	S
241	AATCGA	ייטיייי	СТСС	ልርጥርር	ۍ.	שייירי	ኮሮርር	ר יייי	TC	ጥርር	ጋጥ 4	ירפ	ርሞጥር	ጥርር	CAC	CCA	ኮጥጥረ	ጉልርጥ
	TTAGCT																	
58	N R	F S	G	V I	•	S	R	F	S	G	S	G	S	G	${f T}$	D	F	T
201	000100		<b>6010</b>															
301	CTGACC																	
78	L T			L (		P		D		acu A				C C	AAG S	0	S	T T
				-								_	_	_	-	~	-	-
361	CATGTC																	
0.0	GTACAG H V					_												
96	п V	РЬ	1	F C	,	Q	G	T	Λ.	V	Ľ	_	K	R	Т	V	Α	Α
421	CCATCT	GTCT	TCAT	CTTC	C	GCC	ATC:	ГGАТ	GA	GCA	GTT	GA	AATC	TGG.	AAC	TGC	rrc?	GTT
	GGTAGA	CAGA	AGTA	GAAGO	G	CGG.	rag <i>i</i>	ACTA	CT	CGT	CAA	CT	TTAG	ACC'	TTG	ACGA	\AGI	ACAA
118	P S	V F	Ι	F I	•	P	S	D	E	Q	L	K	S	G	T	A	S	V
481	GTGTGC	CTGC	TGAA	TAACI	т	CTAT	rcco	CAGA	GA	GGC	CAA	AG	TACA	GTG	GAA	GGTC	iga 1	TAAC
	CACACG																	
138	A C	L L	N	N F	•	Y	P	R	E	A	K	V	Q	W	K	V	D	N
E / 1	CCCCTC	יר א א מי	cccc	m a a .~n		CCAC	~~ ~ ~	7 X C/M	CIT!	~ » ~	202	~~	1001	C	~ ~ ~ ~	0010		
241	GCCCTC																	
158	A L																	
601	TACAGO																	
178	ATGTCG Y S			GTGGC T I				STCG						CTT" K			rcae V	
			Ū		•	•	_	•	•	••	_	•	~		••	K	•	•
661	GCCTGC																	
100	CGGACG																	
138	A C	r A	T	н с	2	G	ь	5	S	ħ	V	Т	K	S	F.	N		_
721	GAGTGT	TAAG	CTGA	TCCTC	T	ACG	CCGC	GACG	CA	TCG'	TGG	CC	CTAG'	TAC	GCA	(SEQ	א עו עו עו	U.34) :GTA
	CTCACA	ATTC	GACT	AGGAC														
218	E C	O (SEC	ID NO	.51)			_			_	_							

FIG. 31B



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Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Light Chain

LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSL@PEDFATYYCSQST HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLINNFYPREAKVQWKVDN **ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG** MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTY EC (SEQ ID NO.51) Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Heavy Chain

WVKQ**A**PGKGLEWVGYIDPSNGETTYNQKFKGRFT**L**SRDNSKNT**A**YLQMNSLRAEDTAVYY CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK MKKNIAFLLASMFVFSIATNAYAEVQLVESGGGLVQPGGSLRLSCAASGYSFSSHYMH VDKKVEPKSCDKTHT (SEQ ID NO.55)

# FIG. 31C

# ANTIBODY FRAGMENT-POLYMER CONJ. UGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL NOTIBODIES Hsei et al. Appl. No.: 09/234,182 Atty Docket: GENENT.093A





ANTI-IL-8 MONOCLONAL ANTIBODIES

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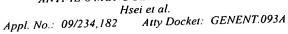


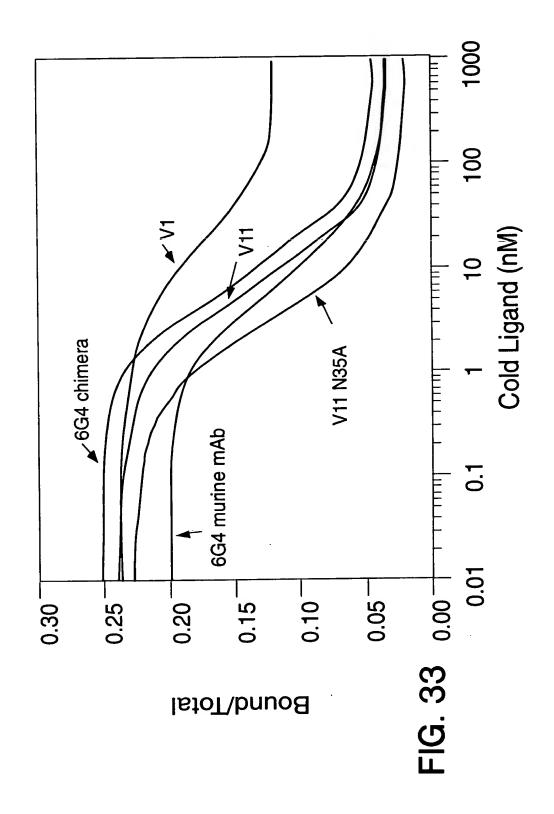
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FIG. 32



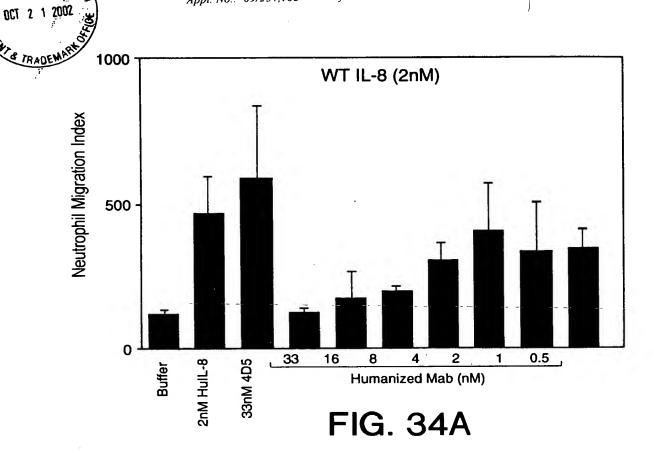






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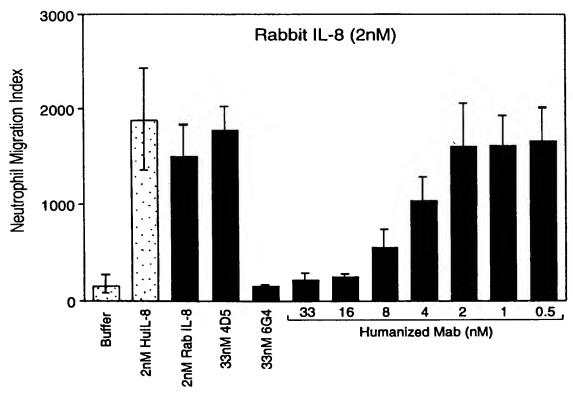
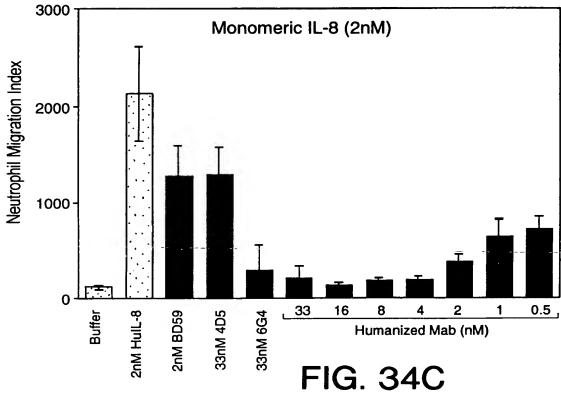
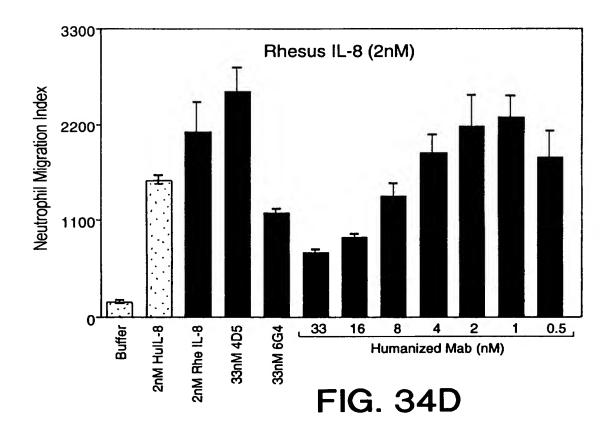


FIG. 34B



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anti-IL-8 6G4.2.5V11N35A Light Chaim Amino Acid Sequence of the humanized

HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN **ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG** MKKNIAFLLASMFVFSIATNAYADIOMTQSPSSLSASVGDRVTITCRSSQSLVHGIGATY LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQST EC (SEQ ID NO.56) Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Heavy Chain

**WVRQAPGKGLEWVGYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLOMNSLRAEDTAVYY** CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK MKKNIAFLLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH VDKKVEPKSCDKTHT (SEQ ID NO.52) Amimo Acid Sequence of the putative Pepsin Cleavage Site and GCN4 Leucine Zipper

CPPCPAPE<u>LL</u>GGRMKQLEDKVEELLSKNYHLENEVARLKKLVGER (SEQ ID NO.57)

FIG. 35

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# ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES Hsei et al.

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1	ATGAA		CA	አጠአጠ	ccc	N TOTO	mem	וייינו	TCC A	mc/	ጉ አ ሙ	nmm.	~~	mmmm	mmc	<b>መ</b> ልመ	TTC:C	ma c	8 8 8 C
_	TACTI																		
-23	M K													F					
61	GCATA																		
_	CGTAT																		
-3	A Y	Α	D	Ι	Q	M	Т	Q	S	P	S	S	L	Ş	Α	S	. <b>V</b>	G	D
121	AGGGT	CAC	CA	TCAC	СТС	CAG	GTC	AAG	rcaa.	AG	CTT	AGT.	AC	ATGG	тат	AGG	TGC	TAC	GTAT
	TCCCA										-								
18	R V													G					
181	TTACA																		
	AATGI																		
38	L H	W	Y	Q	Q	K	P	G	K	Α	P	K	L	L	I	Y	K_	<u>_V_</u>	_S _.
241	AATCG	ATT	СТ	CTGG	AGT	CCC	TTC	rcge	CTTC	TC	TGG	ATC	CG	GTTC	TGG	GAC	GGA'	TTT(	САСТ
	TTAGO																		
58	N R	F	S	G	$\mathbf{v}$	P	S	R	F	s	G	s	G	S	G	${f T}$	D	F	T
301	CTGAC																		
	GACTO																		
78	L T	I	S	S	L	Q	P	E	D	F	A	Т	Y	Y	С	<u>s</u>	Q	<u>s</u>	<u>T</u>
361	CATGI	rece	CC	TCAC	വസസ	TCC	ACA(	יככי	דמרר	220	<b>ጋር</b> ጥ	2C A	CA	ጥር ል ል	ACG	מממ	ጥርጥ	GGC'	TCCA
361	GTACA																		
98	H V																v		
		_	-		_		_	_	-										
421	CCATC																		
	GGTAG									,							ACG.	AAG	ACAA
118	P S	V	F	I	F	P	P	S	D	E	Q	L	K	S	G	Т	A	S	V
481	GTGTG	ירטים	יכר	тсаа	ጥልል፡	்புரா	СТА	rcc	CAGA	GAG	GGC	CAA	AG	TACA	GTG	GAA	GGTY	GGA'	TAAC
101	CACAC															-			
138	v c	L	L	N	N	F	Y	P	R	E	A	K	V	Q	W	K	V	D.	N
541	GCCCI				-														
	CGGGA																		GTGG
158	A L	Q	S	G	N	S	Q	E	S	V	T	E	Q	D	S	K	D	S	T
601	TACAC	בררית	מיי	CCAG	CAC	ССФ	GAC	<u>ጉ</u> ርጥ(	2260	<b>A A</b> :	ACC:	ACA.	СТ	ACGA	GAA	ACA	CAA	AGTY	СТАС
001	ATGTO																		
178	Y S										A				K		K		
661	GCCTC																		
	CGGAC																		
198	A C	E	V	T	H	Q	G	L	S	S	P	V	T	K	S	F		R	_
701	GAGTO	ء سالان	20	CITICS =	mcc.	mom	300	200	2200	CN	TOO	T/-	cc	CMAC	መአ 🗸	CCX			1O.58)
121				GACT															
212	E C			ID NO		UM	130	٠٠٠٠	-130	31/			<b></b>	GAIC	410	<b>-91</b>	IGA	·	-CMI
210		•	,000	, 10 110	.50)			<u></u>											

FIG. 36

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# ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES

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DEMP																			
781	AAAAG	GGT	ΑТ	CTAG	AGG'	TG	AGG'	rga'i	TTTT	YTA	GAA	AAA	GA	ATAT	CGC	ATT	TCTI	CTI	'GCA
	TTTTC	CCA	TA	GATC'	TCC	AAC	TCC	ACT	AAA	TAC	CTT	TTT	CT	TATA	GCG'	TAA	<b>AGA</b>	AGAA	CGT
-1														I					
-														_		_	_		
0.41	тстат		~~	mmmm	mmor	n 2 m	maan	na		000	~m ».		ma	a com	mc a	CCM	х сто	יראר	ישכישי
841																			
	AGATA																		
-11	S M	F	V	F	S	I	A	T	N	Α	Y	Α	E	V	Q	L	V	Q	S
901	GGCGG	יתיכה	ברכ	тсст	GCAC	300	AGGG	366	тса	СТС	CCG	ጥጥጥ	GТ	CCTG	TGC	AGC	TTC	rggo	TAC
701	CCGCC																		
_																			
8	G G	G	Ь	V	Q	Р	G	G	S	L	R	L	S	C	Α	Α	5	<u>.G</u>	<u>.x</u>
961	TCCTI	CTC	GA	<b>GTCA</b>	CTA?	TAT	GCA	CTG	GTC	CG'	rca(	GGC	CC	CGGG	TAA	GGG	CCTC	<b>GA</b>	\TGG
	AGGAA	GAG	CT	CAGT	GAT	ATA	CGT	GAC	CCAG	GC	AGT	CCG	GG	GCCC	ATT	CCC	GGA	CTI	ACC
2.8	S F	S	S	н	Y	М	н	W	v	R	O	A	P	G	K	G	L	E	W
	~							••	•		-		_	_		_	_	_	••
1001	ammaa		<b></b>	mmo N	maar	nma	O 3 3 1	TO 01	n ~ 3 3	3.00	n 2 🔿	om a i	T1 2	a mo a			C2 20	7000	CCM.
1021	GTTGG																		
	CÃÃCC																		
48	V G	Y_	I	D	P	S	N	G	E	T.	T	Y	_N_	0	_K_	F	K	G	R
1 0 9 1	TTCAC	הינותים	יים מי	СТСС	CGA	ממי	CTC	ממה	מממ	ΔC	മേന	מתמ	CC	тсса	СДТ	CAA	CAGO	יריתי	CCT
1001	AAGTO																		
																		,	
68	F T	L	S	R	D	N	S	K	N	$\mathbf{T}$	Α	Y	L	,Q	M	N	s	L	R
1141	GCTGA	AGGA	CA	CTGC	CGT	CTA	TTA	CTG'	TGCA	AG.	AGG	GGA'	TT	ATCG	CTA	CAA	TGG:	rga(	TGG
	CGACT	רכת	יתי	GACG	GCA	ጥልድ	ААТ	GAC	ACGT	TC	TCC	ССТ	AA	TAGO	САТ	GTT	ACC	АСТО	ACC
0.0	A E																		
00	A E	ע	1	A	٧	I	ĭ	C	A	К	<u>u</u>						G		_11
1201	TTCT																		
	AAGA/	AGCI	GC.	<b>AGAC</b>	CCC	AGT	TCC'	TTG	GGAC	CA	GTG	GCA	GA	GGAG	CCG	GAG	GTG	GTT(	CCCG
108	F F	D	V	W	G	0	G	${f T}$	L	V	$\mathbf{T}$	V	S	S	Α	S	${f T}$	K	G
						_													
1261	CCATO	CCT	тОт	TCCC	ССТ	266	ACC	כיייכי	יחייים	ΔΔ	CAC	CAC	СT	СТСС	יכככ	CAC	AGC	300	יכיתכ
1201	GGTA																		
		_																	
128	P S	V	F	P	L	Α	P	S	S	K	S	$\mathbf{T}$	S	G	G	$\mathbf{T}$	Α	Α	ь
1321	GGCT	GCC1	rgg	TCAA	GGA	CTA	CTT	CCC	CGAA	CC	GGT	GAC	GG	TGTC	GTG	GAA	CTC	AGG	CGCC
	CCGA																		
140	G C																S		
148	G C	Ţ	٧	K	ט	Y	r	P	E	P	V	1.	V	3	W	IA	3	G	A
1381	CTGA	CCAC	3CG	GCGT	'GCA	CAC	CTT	CCC	GGCT	GT	CCT	ACA	GT	CCTC	AGG	ACT	CTA	CTC	CCTC
	GACT	GGTC	CGC	CGCA	CGT	GTG	GAA	GGG	CCGA	CA	GGA	TGT	CA	GGAG	TCC	TGA	GAT	GAG	GAG
169	L T																		
100	D .	3	G	•	11	•	•	•	-	•		×	_		•	~	•	_	_
																~~~			
1441	AGCA																		
				ACTG															
188	s s	v	V	T	v	P	S	S	S	L	G	\mathbf{T}	Q	\mathbf{T}	Y	I	C	N	V
	_												-						
1501	AATC	מראי	AGC	CCAC	א מים:	CAC	CDA	ርርጥ	CGAC	A A	GA A	ልርጥ	באתי	AGCC	מ מיםי	ΑπС	ጥጥር፣	TGA	מממר
TOOT				GGTC															
208	N H	K	P	S	N	${f T}$	K	V	D	K	K	V	E	P	K	S	C	ט	K
1561	ACTC	ACA	CAT	GCCC	GCC	GTG	CCC	AGC	ACCA	GA	ACI	GCT	'GG	GCGG	CCG	CAT	GAA	ACA	SCTA
				CGGG															
220	T H																		
220	1 n	1	C	E	E	_	-	••	-				-		- `			**	_
											_								

FIG. 37A



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1621 GAGGACAAGG TCGAAGAGCT ACTCTCCAAG AACTACCACC TAGAGAATGA AGTGGCAAGA CTCCTGTTCC AGCTTCTGA TGAGAGGTTC TTGATGGTGG ATCTCTTACT TCACCGTTCT 248 E D K V E E L L S K N Y H L E N E V A R

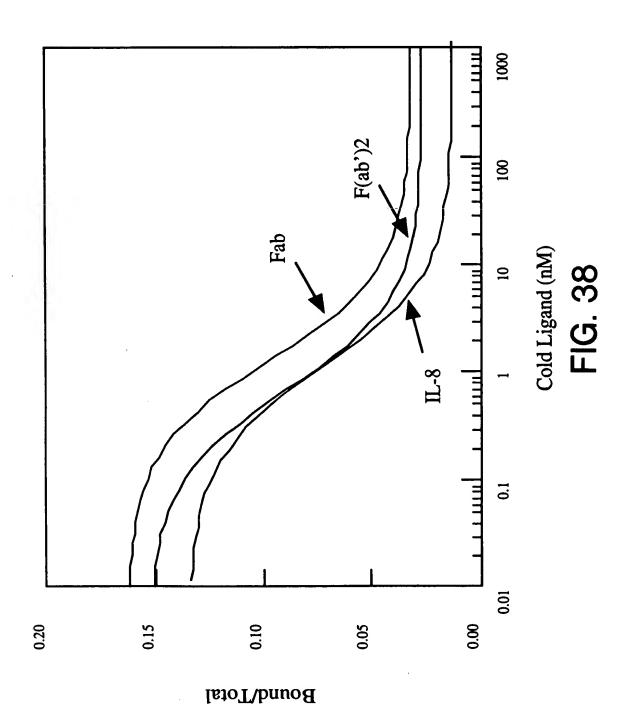
1681 CTCAAAAAGC TTGTCGGGGA GCGCTAA (SEQ ID NO.59)
GAGTTTTCG AACAGCCCCT CGCGATT

68 L K K L V G E R O (SEQ ID NO.60)

FIG. 37B



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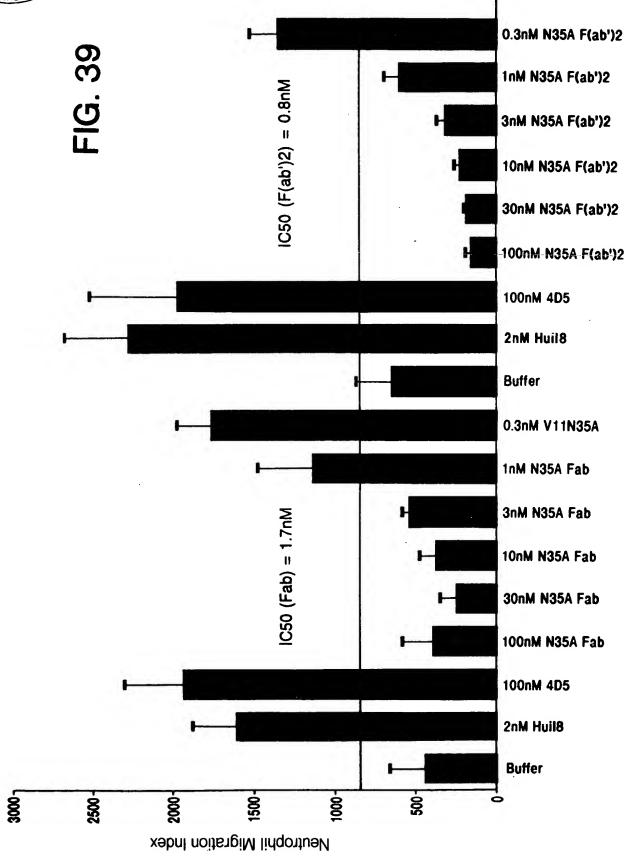


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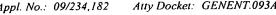
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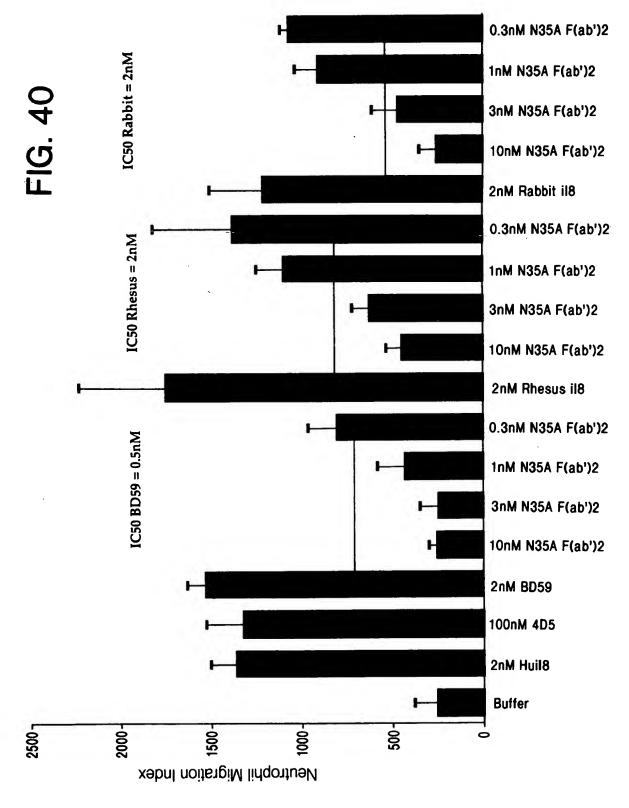
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ANTI-IL-8 MONOCLONAL ANTIBODIES

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mnlI

fnu4HI bstUI snaBI

bsoFI bbvI

hinPI bsaAI bsh1236I

hhaI/cfoI

aluI

DSmI

cacli sfaNI

hhal/cfol mull haell csp61

rsal

hinPI

fokI sfani

201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA CCCGCGACAT GCTCCATTIC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT aluI



pleI

aluI

ARI						
hindIII mboli taqı ddel tru91 earl/ksp6321 earl/ksp6321 earl/ksp6321 msel cac81 mboli hinfi hinfi hinfi aatacagac atgaaadatc tcattgctga gttgttatt aagcttgccc aaaaagaaga agagtcgaat ttatgtctg tacttttag agaacgact caacaataaa ttcgaacgg tttttcttct tcttata	sau3AI mbol/ndeII[dam-] dpnI[dam+] maeIII bsrDI hhal/cfoI nspBII bclI[dam-] ATTATCGTCA CTGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGGG TAATAGCAGT GACGTTATAC CGCGTTTTAC TGGTTGTCCC CAACTAACTA GTCCATCTCC					
hindIII tru9I msel cac8I TT AAGCTTGCC	acil nspBII ACCAACAGGG TGGTTGTCGC					-
tri ms GTTGTTATTT CAACAATAAA	hinPI hhal/cfoI GCGCAAAATG CGCGTTTTAC	thaI	fnuDII/mvnI	н		maeII
ddeI bsrDI TCATTGCTGA AGTAACGACT	TCGCAATATG AGCGTTATAC	Ē.	4	fpu4HI	bsoFI	Ivdd
TTGGATAAGG AACCTATTCC	aluI indIII AGCTTTGGAG TCGAAACCTC					
ecori apol bsli GAATTCAACT TCTCCATACT TTGGATAAGG CTTAAGTTGA AGAGGTATGA AACCTATTCC	bspMI hinPI hhal/cfoI mstI aviII/fspI hindIII GAACTGTGTG CGCAGGTAGA AGCTTTGGAG					
ecoRI pflMI apol bsll 1 GAATTCAACT TCTCCATACT TTGGATAAGG CTTAAGTTGA AGAGGTATGA AACCTATTCC	bspMI hinPI hhal/cfoI mstI aviII/fspI hindIII 101 GAACTGTGTG CGCAGGTAGA AGCTTTGAG CTTGACACAC GCGTCCATCT TCGAAACCTC					

hgiAI/aspHI ecl136II bsp1286 **bsinka**I hgiJII sstI bmyI BacI tadI ecoRI bfaI rmaI mael tru9I mseI ahdI/eam1105I eagl/xmalll/eclXI haeIII/palI bsmAI bsiEI cfrI mcrI eaeI maelli nspBII IInad aluI

maelli apol banii

TITICAAITA GAAAAGITGI CGACAGIAII ICAACAGIGC CGGCICIGAA IAICAGCGAA ACAAAAAIAA AAAAIIACAI AAACAIIGAI CIIAAGCICG

301 ABANGITAAT CTITICAACA GCTGTCATAA AGTTGTCACG GCCGAGACTI ATAGTCGCTT TGTTTTTTTT TTTTAATGTA TTTGTAACTA GAATTCGAGC

tru9I nseI

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401 TCGGTACCCG GGGATCCTCI CGAGGTTGAG GTGATTTTAT GAAAAAGAAT ATCGCATTTC TTCTTGCATC TATGTTCGTT TTTTCTATTG CTACAAACGC AGCCATGGGC CCCTAGGAGA GCTCCAACTC CACTAAAATA CTTTTTCTTA TAGCGTAAAG AAGAACGTAG ATACAAGCAA AAAAGATAAC GATGTTTGCG The penultimate nucleotide was changed fr G toT ^ SIA M F V L A S sfani Iloqu a mutation was found that inactivated the mluI site. K K N alwI[dam-] mnlI nlaIV paeR7I kpnI cauII dpnII[dam-] bamHI avaI bstYI/xhoII bani bsaJi alwi[dam-] asp718 acc65I hgiCI nlaIV

mbol/ndeII[dam-]

dpnI[dam+]

csp6I

rsaI

sau3AI taqI

avaI

moli

xhoi

caull bsaJI

dsav

ncil

xmaI/pspAI

scrFI

SmaI

hpall

dsav

SCLFI

ncil

nlaIII 1 ATACGCTGAT ATCCAGATGA CCCAGTCCCC GAGCTCCCTG TCGCCTCTG TGGGCGATAG GGTCACCATC ACCTGCAGGT CAAGTCAAAG CTTAGTACAT TATGCGACTA TAGGTCTACT GGGTCAGGGG CTCGAGGGAC AGGCGGAGAC ACCCGCTATC CCAGTGGTAG TGGACGTCCA GTTCAGTTTC GAATCATGTA hindIII csp6I rsaI ddeI aluI bspMI sse8387I scfI pstI bstEII hphI bsgI bspMI maeIII mpli acil hgiAI/aspHI ec1136II bsp1286 bsinkal hgiJII bsrI aval aluI banII saci bmyI tth11111/aspI bsmFI ecoRV

FIG. 41B

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Atty Docket: GENENT.093A Appl. No.: 09/234,182



SCLFI

scal plail TGGATCCGGT TCTGGGACGG ATTTCACTCT GACCATCAGC AGTCTGCAGC CAGAAGACTT CGCAACTTAT TACTGTTCAC AGAGTACTCA GAGCGAAGAG ACCTAGGCCA AGACCCTGCC TAAAGTGAGA CTGGTAGTCG TCAGACGTCG GTCTTCTGAA GCGTTGAATA ATGACAAGTG TCTCATGAGT 601 GGTATAGGTG CTACGTATTT ACACTGGTAT CAACAGAAAC CAGGAAAAGC TCCGAAACTA CTGATTTACA AAGTATCCAA TCGATTCTCT GGAGTCCCTT CCATAICCAC GAIGCAIAAA IGIGACCAIA GIIGICIIIIG GICCIIIICG AGGCIIIGGI GACIAAAIGI IICAIAGGII AGCIAAGAGA CCICAGGGAA ACCTITGGAC AGGGTACCAA GGTGGAGATC AAACGAACTG TGGCTGCACC ATCTGTCTTC ATCTTCCGG CATCTGATGA GCAGTTGAAA CCACCTCTAG TTTGCTTGAC ACCGACGTGG TAGAAGGGGCG GTAGACTACT CGTCAACTTT csp6I rsaI hinfI bpmI/gsuI[dcm-] **DSmFI** clal/bsp106 bspDI[dam-] Ø tfiI U s S II oqu Iloqu bpuAI E D bbsI bpuAI mboli ppsI fnu4HI SIDP bsoFI bbvI fnu4HI scfI pstI Ipsq bsoFI bbvI mbol/ndell[dam-] aluI RTV ß apyI[dcm+] T I dpnII[dam-] U dpnI[dam+] ecoRII bstNI mvaI dsav sau3AI ø bsaJI TGCAAACCTG TCCCATGGTT G T D styI X csp6I asp718 DSmFI acc651 rsaI hgiCI nlaIV mbol/ndeII[dam-] kpnI banI U dpnII[dam-] alwI[dam-] bstYI/xhoII dpnI[dam+] alwI[dam-] hpail TYL Idsm bsli bsaWI U sau3AI nlaIV ဟ bamHI maeII 801 TGTCCCGCTC 701 CICGCIICIC ACAGGGCGAG berBI acil Œ bsmFI н g 99 66

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Atty Docket: GENENT.093A Appl. No.: 09/234,182

maeIII apyI[dcm+] ecoRI1 **b**stNI cac8I dsaV beaJI GGAGGTTAGC CCATTGAGGG 1001 AGGAGAGTGT CACAGAGCAG GACAGCAAGG ACAGCACCTA CAGCCTCAGC AGCACCTGA CGCTGAGCAA AGCAGACTAC GAGAAACACA AAGTCTACGC 901 TCTGGAACTG CTTCTGTTGT GTGCCTGCTG AATAACTTCT ATCCCAGAGA GGCCAAAGTA CAGTGGAAGG TGGATAACGC CCTCCAATCG GGTAACTCCC TCCTCTCACA GIGICTCGIC CIGICGIICC IGICGIGGAI GICGGAGICG ICGIGGGACI GCGACICGII ICGICTGAIG CICTIIGIGI IICAGAIGCG S a moli ball CACGGACGAC TTATTGAAGA TAGGGTCTCT CCGGTTTCAT GTCACCTTCC ACCTATTGCG Ø A D Y z Ω blpI/bpull02I cell1/espI X hgaI ddeI csp6I rsal haeIII/palI TLT REAKV fpu4BI haeI **bsoFI** mpli mall bbvI r S ddeI p. တ scfI asp700 S XmnI cac81 aluI C II II cac8I AGACCTTGAC GAAGACAACA > > maeIII asp700 GT ဟ S

132

BCLFI

mvaI

haeIII/palI bfaI nael Thai sau96I hgaI Idsm mbol/ndeII[dam-] dpnII[dam-] aluI dpnI[dam+] mpli sau3AI tru9I

1101 CIGGGAAGIC ACCCAICAGG GCCIGAGCIC GCCGICACA AAGAGCIICA ACAGGGGAGA GIGIIAAGCI GAICCICIAC GCGGACGCA ICGIGGCCCI

aluI

maeIII

ecc01091/drall

alwNI[dcm-]

maelli

asul ddel

hgiAI/aspHI

hgiJII

sstI sacī ecl136II bsp1286

bsinkAI

bmyI

haeIII/palI sau96I banII TICICGAAGI IGICCCCICI CACAAIICGA CIAGGAGAIG CGGCCIGCGI AGCACCGGGA

o (SEO ID NO.56)

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CGGCCAGTGT

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GACGCITCAG IGGGIAGICC CGGACICGAG

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hpaII sfaNI

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Hsei et al.

Atty Docket: GENENT.093A ppl. No.: 09/234,182

TPERM	ANTIBODY
1212	App
TRADEMARKS	

			mboli sfani	ITCTTGCATC TATGTTCGTT TTTTCTATTG AAGAACGTAG ATACAAGCAA AAAAGATAAC	LASMFVFSIA								aluI	alwNI[dcm-]	fnu4HI	bsoFI	bbvI	CCGITIGICC IGIGCAGCIT CIGGCIACIC	GCCAAACAGG ACACGTCGAA GACCGATGAG	R L S C A A S G Y S	
		hI	[OQW I]	1201 AGTACGCAAC TAGTCGTAAA AAGGGTATCT AGAGGTTGAG GTGATTTTAT GAAAAAGAAT ATCGCATTC TTCTTGCATC TATGTTCGTT TTTTCTATTG TCATGCGTTG ATCAGCATTT TTCCCATAGA TCTCCAACTC CACTAAAATA CTTTTTCTTA TAGCGTAAAG AAGAACGTAG ATACAAGCAA AAAAGATAAC	M K K N I A F L L A S M F V F S I A	SCIFI	mvaI	ecoRII	dsaV	scrFI	mval fnu4HI	ecoRII	dsav bstNI hgiJII	bstNI bsoFI bsp1286	apy1[dcm+] bsaJI bmyI	haeIII/pall apyI[dcm+]	acil hael bbvI banII	1301 CTACAAACGC GTACGCTGAG GTTCAGCTAG TGCAGTCTGG CGGTGGCCTG GTGCAGCCAG GGGGCTCACT CCGTTTGTCC TGTGCAGCTT CTGGCTACTC	c eccaccegac cacercegre cecegagida (TNA YAE VOLV OSGGGL VOPGGSL RLS CAAS GYS	
75117	maeI	bfaI	xbal mull mull	AA AAGGGTATCT AGAGGTTGA(FT TTCCCATAGA TCTCCAACT(rmaI	maeI	nli bfai	I aluI	AG GITCAGCIAG IGCAGICIG	IC CAAGICGAIC ACGICAGAC	S O A I O A	
TOMT	mael	rsal bfal	csp6I speI	1201 AGTACGCAAC TAGTCGTAA	-23					rsal	llgs/IWI/spli	thal	fnuDII/mvnI	bstui	bsh1236I	mluI csp6I mnlI	afliii ddei	1301 CTACAAACGC GTACGCTG1	GATGTTTGCG CATGCGACT	-5 T N A Y A E	

scrFI
ncil
mspi
hpail
dsav
cauli
bsli
xmal/pspAi
smal
ncil
dsav
cauli

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES Hsei et al. Appl. No.: 09/234,182 Atty Docket: GENENT.093A .

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OCT 2 1 2002
PADEMARK SET

EMARKO		φ.	dra
bsli dell[dam-] dpn[[dam+]	cac8I mnli cac8I ddel drdi GCCTGCGTGC TGAGGACACT GCCGTCTATT CGGACGCACG ACTCCTGTGA CGGCAGATAA L R A E D T A V Y Y	sau961 haeIII/palI sau961 nlaIV hgiJII bsp1286 bsp1201	mval mnll banil ecorii bsaji asui sati dsav bseri apai sati bstni esp3i styl asui bsaji hphi bsmbi mnli bsaji nlaiv apyi[dcm+] bsmAi haelii/pali ecol091/drali TGGGTCAAG GAACCTGGT CACCGTCTC TCGGCTCCA CCAAGGGCCC ACCCCAGTTC CTTGGGACCA GTGGCAGGG AGCCGGAGGT GGTTCCCGGG W G Q G T L V T V S S A S T K G P seq right is from p6G425chim2.fab2 ^
snaBI hphi ATGGTGAAAC TACCACTTTG	mpli ddei drdi c TGAGGACAC G ACTCCTGTG		as ap mnli haeIII/pa TCGGCCTCCA AGCCGAGGT S A S T
bsli sau3AI mbol/ndeli[dam-] dpnl[dam-] snaBI alw1[dam-] hphI ATATT GATCCTTCCA ATGGTGAAAC TATAA CTAGGAAGGT TACCACTTTG I D P S N G E T	cac81 cac81 de GCCTGCGTGC CGGACGCACG	maeIII stEII	mval mnli ecorii bsaji dsav bseri bstni espji bsaji hphi bsmbi apyi[dcm+] bsmAi CCCTGGT CACCGTCTC TGGGGACCA GTGGCAGGG AGGCAGGG AGGCAGGG AGGGACCA GTGGCAGGG AGGGACCA GTGGCAGGG AGGGACCA GTGGCAGGG AGGGACCA GTGGCAGGG AGGGACCA GTGGCAGGG AGGGACCA GTGGCAGGG AGGGGACCA GTGGCAGGG AGGGACCA GTGGCAGGGACCA GTGGCAGGGACCA GTGGCAGGGACCA GTGGCAGGGACCA GTGGCAGGACCA GTGGCAGGGACCA GTGGCAGGACCA GTGGCAGGACCA GTGGCAGGACCA GTGGCACCA GTGGCACCA GTGGCACCA GTGGCACCA GTGGCACCA GTGGCACCA GTGCCACCA GTCCACCA GTGCCACCA GTCCACCA GTCCACCACCA GTCCACCACCA GTCCACCACCA GTCCACCACCA GTCCACCACCA GTCCACCACCA GTCCACCACCACCA GTCCACCACACA GTCCACCACCACCACCACACA GTCCACCACACA GTCCACCACACACA GTCCACCACACACA GTCCACCACACACA GTCCACCACACACACACACACACACACACACACACACACA
	PAGATGAACA STCTACTTGT OMNS	maeII bstEII scrFI	mval mnli ecoRII bsaJI asu dsaV bseRI batNI esp3I spaJI bsaJI hphI bsmBI mnlI b nlaIV apyI[dcm+] bsmAI haeIII/pal G GAACCCTGGT CACCGTCTC TCGGCCTCCA C C CTTGGGACCA GTGGCAGGGT G G T L V T V S S A S T seq right is from p6G425chim2.fab2
bsaJI dsaV avaI bstNI bsaJI bslII sau96I apyI[dcm+] nlaIV sau96I mboI/r haeIII/palI asuI ecol09I/draII haeIII/palI TCAGCCCCG GGTAAGGGC TGGAATGGGT TGGATATATT AGTCCGGGC CCATTCCCGG ACCTTACCA ACCTATATAAA Q A P G K G L E W V G Y I	scfi psti bsgi bspMi AGCATACCTG (mval mnl ecoRII bsaJI dsaV bseRI bsaHI bsaJI bstNI esp3I bsaJI hphI bsmBI nlaIV apyI[dcm+] bsmAI TGGGTCAAG GAACCTGGT CACGTCTCC ACCCAGTTC CTTGGGACCA GTGGCAGGG W G Q G T L V T V S seq right is from p6G4
bsaJI dsaV avaI bstNI bsaJI bslI sau96I apyI[dcm+ nlaIV haeIII/palI asuI asuI ecol091/draI haeIII/palI AGGCCCG GGTAAGGGC TGGAAF TCCGGGGC CCATTCCCG ACCTTA			
bsaJI avaI bsaJI sau96I nlaIV haeIII/palI asuI eco0109I/dra TCAGGCCCG GGI AGTCCGGGGC CCA	thaI fnuDII/mvnI bstUI bsh1236I nruI T CGCGACAACT CCAAAAACAC 3A GCGCTGTTGA GGTTTTTGTG		maell hinli/s ahall/i taqi hphi bsri mboli aatli G GTGACTGGTT CTTCGACGTC C CACTGACCAA GAAGCTGCAG G D W F F D V
sau96I avaII asuI nlaIV bsrI ACTGGGTCCG TGACCCAGGC	nx CTTTATCT GAAATAGA L S		Ωι
pleI hinfI sau96I taqI avaII xhoI asuI paeR7I nlaIV avaI maeIII bsrI CTTCTCGAGT CACTATATGC ACTGGGTCGG GAAGAGCTCA GTGATATAGG TGACCCAGGC F S B Y M H W V R	haeIII/pali sau96I asuI CAAAAGTTCA AGGGCCGTTT CA GTTTTCAAGT TCCCGGCAAA GT		mD1I ACTGTGCAAG AGGGGATTAT TGACACGTTC TCCCCTAATA C A R G D Y
			mnli 1601 ACTGTGCAAG AGGGATTAT CGCTACAATG TGACACGTTC TCCCCTAATA GCGATGTTAC 96 C A R G D Y R Y N G
1401	1501		1601

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EMARKS ST.	cfr101/bsrF1 bsaW1 tth1111/asp1 ageI maeIII ACC GGTGACGGTG TGG CCACTGCCAC P V T V	maeIII mnli hphi bsp1286 bstEII bmyl bpmI/gsuI[dcm-] rGGTG ACCGTGCCCT ACCAC TGGCACGGGA V T V P S
	mspi hpali bsli GGACTACT TCCCGA CCTGATGA AGGGGCT D Y F P E	fnu4HI bsoFI ddeI /sauI mnlI bbvI I ACTCCCTCAG CAGCG? A TGAGGGAGTC GTCGC? X S L S V
scrFI mval scrFI mval ecoRII dsaV bstNI ecoNI sau96I dsaV	fnu4HI fnu4HI bsoFl bsaJI bsll acil apyl[dcm+] bspl286 asul bsoFl bmyl nspBII bsaJI bbvI apyl[dcm+] ccccACAC CGCCCTCGC CTCCTGCTC AA CCCCGTGTC GCCGGGACCC GACGGACCAG TT G T A A L G C L V K	ddel mpli plei eco811 hinfi scfi bsu361/mstII, ccracaGTCC TCAGGACTC' GGATGTCAGG AGTCCTGAG, L Q S S G L
gang.	fnu4HI AspHI bsolibsaJI bsp1286 acil bsiHKAI bsp1286 asi bmyl mnli bmyl nspBII GAGCACCTCT GGGGCACAG CGG CTCGTGGAGA CCCCGTGTC GCC S T S G G T A A	hgiAI/aspHI bsp1286 bsiHKAI mspI sl hpaII sl scrFI bmyI nciI apaLI/snoI dsav alw44I/snoI cauII GTGCACACCT TCCCGGCTGT CACGTGTGGA AGGGCCGACA
nlaIV hgiCI banI scrFI	ecoRII hgiAI/aspHI dsav bstNI bseRI bsp12 apyI[dcm+] mnlI bsiHK bsaJI mnlI bmyI CCCCTGGCAC CCTCCTCCAA GAGCA GGGGACCGTG GGAGGAGGTT CTCGT P L A P S S K S T hinPI hhaI/cfoI	nlaIV hgiA nari bspl kasi hinli/acyl cac81 hgiCi fnu4HI haeli bsoFI bmyI bani acil apaL ddel ahali/bsaHI nspBII alw4 CT CAGGGGCCT GACCAGGGG GTGC GA GTCCGCGGGA CTGGTCGCG CACG S G A L T S G V H
	mboli bpuAI bbsI 1701 ATCGGTCTTC TAGCCAGAAG	dde 1801 TCGTGGAACT AGCACCTTGA 162 S W N S

CCCGIGGGIC IGGAIGTAGA CGTIGCACTI AGIGITCGGG ICGTIGIGGI ICCAGCIGIT CITICAACTC GGGITTAGAA CACTGITITG G I Q I Y I C N V N H K P S N T K V D K K V E P K S C D K I GGCCACCCAG ACCTACATCT GCAACGTGAA TCACAAGCCC AGCAACACCA AGGTCGACAA GAAAGTTGAG CCCAAATCTT GTGACAAAAC

bsp1286 hgiJII

banII bmyI

styl hincil/hindil

hinfi tfiI

hgiCI banI bsp1286 bmyI

1901 CCAGCAGCTT GGTCGTCGAA S

S

196

bstXI

nlaIV

fnu4BI bsoFI bbvI

maell

bsaJI accI

taqI salI

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SCIFI

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bfaI rmaI nael 2001 TCACACATGC CCGCCGTGCC CAGCACCAGA ACTGCTGGGC GGCCGCATGA AACAGCTAGA GGACAAGGTC GAAGAGCTAC TCTCCAAGAA CTACCACCTA GATGGTGGAT AGTGTGTACG GCCGCCACGG GTCGTGGTCT TGACGACCCG CCGCGTACT TTGTCGATCT CCTGTTCCAG CTTCTCGATG AGAGGTTCTT K earl/ksp6321 E E L aluI **II**oqu tth11111/aspI taqI Δ aluI mnlI 1 E bfaI rmaI maeI nlaIII function between antibody and leucine zipper acil acil fnu4HI **bsoFI** bsiEI eaeI cfrI notI A P E **bsp1286** P P C P nspHI acil bmyI cac8I nlaIII Ideu

eagl/xmall1/eclXI

mcrI

haeIII/palI

fou4HI

bsoFI

GCCGCCGGGC GTTTTTATT CICITACTIC ACCGITCIGA GITITICGAA CAGCCCCICG CGAITCGIAC GCIGCCGGGA ICICAGGGAI IGCGAGCCAA CGGCGGCCCG CAAAAAIAA hpaII cauli Idsm dsaV ncil fnu4HI acil **bsoFI** 2101 GAGAATGAAG TGGCAAGACT CAAAAAGCTT GTCGGGGAGC GCTAAGCATG CGACGGCCCT AGAGTCCCTA ACGCTCGGTT **DamFI** hinfI pleI haeIII/palI bfaI maeI rmaI sau96I asuI o (SEQ ID NO.60) blpI/bpull02I ddeI nlaIII IHdsu cellI/espI eco47III cac8I Igan hhaI/cfoI hinPI haeII V G E R hindIII hinfI pleI

FIG. 41H

GITAACICAT GITIGACAGC ITAICAICGA TAAGCIITAA IGCGGIAGII IAICACAGII AAAITGCIAA CGCAGICAGG CACCGIGIAI GAAAICIAAC CAAITGAGIA CAAACTGICG AAIAGIAGCI AITCGAAAII ACGCCAICAA AIAGIGICAA IIIAACGAII GCGICAGICC GIGGCACAIA CIIIAGAIIG

bspDI[dam-] mseI acil

aluI

hpai nlaili hincii/hindii

2201

tru9I mseI hpaI

clal/bsp106 tru91

aluI taqI hindIII

nlaIV hgiCI

> tru9I mseI

banI

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES Hsei et al. No.: 09/234,182 Atty Docket: GENENT.093A

Appl. No.: 09/234,182



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EM	ART								ATT	TAA						fpu4HI	bsoFI	haeIII/palI	eaeI	cfrI	TGG	ACC
							ecoRV		AT ATCGICC	ra Tagcagg								acil	mcrI	bsiEI	CG ACCGCTT	GC TGGCGAA
haeIII/palI						н	ă	acil	CITGCGGG	GAACGCCC							hgiAI/aspHI	bsp1286	bsiHKAI	bmyI	GCACTGTC	CGTGACAG
	sau96I	SCIFI		mspl mall	hpall	dsaV bslI	cauli	rFI asuI	recesseer	ACGCCCCGGA							hg			EQ I	CGTTCTCGGA	SCAAGAGCCT
	saı		ncil	rsal mspl	csp6I	Idsm	hpall	cfr101/bsrFl asuI	receestac :	ACGGCCATG 1							hinPI	hhaI/cfoI	mstI bslI	aviII/fspI	ATGCGCACC (PACGCGTGG (
				Ä					2301 AATGCGCTCA TCGTCATCCT CGGCACCGTC ACCCTGGATG CTGTAGGCAT AGGCTTGGTT ATGCCGGTAC TGCCGGGCCT CTTGCGGGAT ATCGTCCATT	TTACGCGAGT AGCAGTAGGA GCCGTGGCAG TGGGACCTAC GACATCCGTA TCCGAACCAA TACGGCCATG ACGGCCCGGA GAACGCCCTA TAGCAGGTAA										sfani	2401 CCGACAGCAT CGCCAGTCAC TATGGCGTGC TGCTAGCGCT ATATGCGTTG ATGCAATTTC TATGCGCACC CGTTCTCGGA GCACTGTCCG ACCGCTTTGG	GCTGTCGTA GCGGTCAGTG ATACCGCACG ACGATCGCGA TATACGCAAC TACGTTAAAG ATACGCGTGG GCAAGAGCCT CGTGACAGGC TGGCGAAACC
_							Ŧ	scfI	CTGTAGGCAT	GACATCCGTA			ifol					11			ATATGCGTTG	TATACGCAAC
sfaNI	SCLFI	mvaI	ecoRII	dsaV	bstNI	bsaJI	hphI apyI[dcm+]	III foki scfI	ACCCTGGATG	TGGGACCIAC	•	hinPi	hhaI/cfoI	rmaI	maeI	nheI	fnu4HI haeII		bbvI bfaI	cac8I	TGCTAGCGCT	ACGATCGCGA
					nlaIV.	mnll hqiCI	1	banı maelii	CGCACCGTC	SCCGTGGCAG							for	psq	rdd V	cac8I	TATGGCGTGC	ATACCGCACG
						ILum	bsaJI	hhal/cfol fokl	CGTCATCCT	GCAGTAGGA									maeIII	bsrI	GCCAGTCAC	SCGCTCAGTG
							hinPI	hhaI/cfol	ATGCGCTCA 1	TACGCGAGT A										sfaNI bsrI	CCACAGCAT (GCTGTCGTA C
									2301 2	•											2401 (

hgaI Idsm mbol/ndeII[dam-] dphil[dam-] bstYI/xhoII dpnI[dam+] alwI[dam-] sau3AI nlaIV bamHI mbol/ndeII[dam-] dpnII[dam-] dpnI[dam+] bstUI nlaIII bsh1236I fnuDII/mvnI sau3AI

moli

hpall sfaNI CCCCCCCCA GICCIGCICG CIICGCIACI IGGAGCCACI AICGACIACG CGAICAIGGC GACCACACCC GICCIGIGGA ICCICIACGC CGGACGCAIC GCCGCCCCCCT CAGGACGAGC GAAGCGATGA ACCTCGGTGA TAGCTGATGC GCTAGTACCG CTGGTGGGG CAGGACACCT AGGAGATGCG GCCTGCGTAG alwI[dam-] bslI taqI nlaIV cac8I acil bsrI 2501

acil fnu4HI bsoFI

FIG. 4

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bmyI bspHI hhal/cfoI eco47III rcal hinPI haeII 2601 GIGGCCGGCA TCACCGGCGC CACAGGIGCG GIIGCIGGCG CCTAIAICGC CGACAICACC GAIGGGGAAG AICGGGCICG CCACIICGGG CICAIGAGCG CACCGCCGT AGIGGCCGCG GIGICCACGC CAACGACCGC GGAIAIAGCG GCIGIAGIGG CIACCCCIIC IAGCCCGAGC GGIGAAGCCC GAGIACICGC banII nlaIII bsp1286 hqiJII mbol/ndeII[dam-] **bsp1286** sau3AI cac8I hgiJII dpnII[dam-] banII bmyI dpnI [dam+] mboII[dam-] Ihqd ahaII/bsaHI hinl1/acy1 nlaIV hgiCI haeII BCLFI kası banI narI ncil cac8I acil hphI ahaII/bsaHI hinl1/acy1 cfri sfaNI cfr101/bsrFI hgici haeII cfr101/bsrFI banI haeIII/pall hpaII Idsm hpall cac8I Idem naeI eaeI

hhaI/cfoI

hinPI

hhaI/cfoI

nlaIV

kası

narI

hinPI

bsoFI hgiAI/aspHI **bsp1286 DSIHKAI** bmyI aciI fnu4HI aciI fpu4BI bsoFI bslI aciI cac8I ahaII/bsaHI hinl1/acy1 haeII hqiCI narI kası banI **bsmFI** haeIII/palI cauli asul bsaJI bsaJI ecc01091/drall cac8I bslI cfrI haeIII/palI bslI sau96I nlaIV

hhai/cfoi

hpall

Idsm

dsaV

dsaI

nlaIV

hinPI

haeIII/palI GCGCCATCT CCTTGCACGC ACCATTCCTT GCGGCGGCGG TGCTCAACGG GAACAAAGCC GCACCCATAC CACCGTCCGG GGCACCGGCC CCCTGACAAC CCGCGGTAGA GGAACGTGCG TGGTAAGGAA CGCCGCCGCC ACGAGTTGCC 2701 CITGITICGG CGTGGGTAIG GIGGCAGGCC CCGIGGCCGG GGGACTGIIG

2801 CCTCAACCTA CTACTGGGCT GCTTCCTAAT GCAGGAGTCG CATAAGGGAG AGCGTCGTCC GATGCCCTTG AGAGCCTTCA ACCCAGTCAG CTCCTTCCGG GGAGTIGGAI GAIGACCCGA CGAAGGAITA CGICCICAGC GIAITCCCIC ICGCAGCAGG CIACGGGAAC ICTCGGAAGI IGGGICAGIC GAGGAAGGCC bsrI alul bslI sfaNI hgaI hinfI bslI bsrI bbvI bslI

ecoNI

fnu4HI bsoFI

hpall

bsaWI

FIG. 41J

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moll 2901 resectede scatsactat cstesectea cttatsacts tettettat catscaacte stassacass tseessease setetsset attitesses ban! hpall hhal/cfol cac8I eco47III mspl hinPI cfr101/bsrFI nael haell fpu4HI DSOFI ppvI nlaIV hgiCI nlaIII IIoqu bpuAI bbsI fpu4HI bsoFI acil nlaIII bcgI fnuDII/mvnI bsh1236I hhaI/cfoI bstuI acil hinPI thaI

ACCCGCGCCC CGTACTGATA GCAGCGGCGT GAATACTGAC AGAAGAAATA GTACGTTGAG CATCCTGTCC ACGCCCGTCG CGAGACCCAG TAAAAGCCGC

thal

TCGCTGGAGC GCGACGATGA TCGGCCTGTC GCTTGCGGTA TTCGGAATCT TGCACGCCCT CGCTCAAGCC TTCGTCACTG GTCCCGGCCAC TCCTGGCGAA AGCGACCTCG CGCTGCTACT AGCCGGACAG CGAACGCCAT AAGCCTTAGA ACGTGCGGGA GCGAGTTCGG AAGCAGTGAC CAGGGCGGTG acil DSMFI sau96I avall nlaIV asuI bsrI maelii cac8I mnlI hinfI aciI cac8I haeIII/palI mbol/ndell[dam-] bpmI/gsuI[dcm-] dpnII[dam-] dpnI[dam+] sau3AI fauDII/mvaI bsh1236I hha I /cfoI bstuI hinPI AGGACCGCTT acil sau96I avaII asuI 3001

bsh1236I foki haeIII/palI thal fnuDII/mvnI bsh1236I mnlI fnuDII/mvnI bstUI bstUI thaI hgaI nruI cac8I maeII fnuDII/mvnI eagI/xmaIII/eclXI hhaI/cfoI **bsh1236I** hinPI bgli nlaiii haeiii/pali bstui thaI acil hgal fnu4HI bsiEI eaeI bsoFI cfrI cfr101/bsrFI haeIII/pall hpaII cac8I Idsm cac8I

MCLI

GTTTGCAAAG CCGCTCTTCG TCCGGTAATA GCGCCCGTAC CGCCGGCTGC GCGACCCGAT GCAGAACGAC CGCAAGCGCT GCGCTCCGAC CTACCGGAAG CECCGGCAIG GCGCCGACG CGCIGGGCIA CGICIIGCIG GCGIICGCGA CGCGAGGCIG GAIGGCCIIC 3101 CAAACGTTTC GGCGAGAAGC AGGCCATTAT

psp1406I

FIG. 41K

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nlaIII

bsiHKAI bmyI cac8I n

fpu4HI

maeIII

dpn1[dam+] nspBII

mbol/ndeII[dam-]

dpnI[dam+]

3301

dpnII[dam-]

taqI[dam-]

bsoFI

bglI

GATCGCTCGC GGCTCTTACC AGCCTAACTT CGATCACTGG ACCGCTGATC GTCACGGCGA TTTATGCCGC CTCGGCGAGC ACATGGAACG GGTTGGCATG

acil dpnII[dam-]

dpnI[dam+]

CTAGCGAGCG CCGAGAATGG TCGGATTGAA GCTAGTGACC TGGCGACTAG CAGTGCCGCT AAATACGGCG GAGCCGCTCG TGTACCTTGC CCAACCGTAC

fnu4HI

bsoFI

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alwI[dam-] 3201 CCCATTATGA ITCITCICGC ITCCGGCGGC AICGGGAIGC CCGCGIIGCA GGCCAIGCIG ICCAGGCAGG IAGAIGACGA CCATCAGGGA CAGCIICAAG GGGTAATACT AAGAAGAGG AAGGCCGCCG TAGCCCTACG GGCGCAACGT CCGGTACGAC AGGTCCGTCC ATCTACTGCT GGTAGTCCCT GTCGAAGTTC bsmFI aluI hgiAI/aspHI bsp1286 bsaJI mpli apyI[dcm+] acil **DSPMI** ecoRII SCIFI sfaNI bshl236I haeIII/palI bstNI dsaV mvaI mbol/ndell[dam-] cac8I nlaIII haeI fnuDII/mvnI sau3AI bstul mbol/ndeII[dam-] acil sau96I cac8I avall sau3AI asuI bsrI foki mslI hpall sfaNI fnu4BI **bsoFI** aciI Idsu fnuDII/mvnI IIoqu sau3AI bsh1236I fau4BI hinfI bsoFI acil bstul thaI cac8I

3401 GATTGTAGGC GCCGCCCTAT ACCTTGTCTG CCTCCCCGCG TTGCGTCGCG GTGCATGGAG CCGGGCCACC TCGACCTGAA TGGAAGCCGG CGGCACCTCG moli hpall nlaIV hgiCI cfr101/bsrFI banI fpu4HI **DSOFI** acil Igem cac8I nael taqI haeIII/palI moli sau96I nlaIV asuI hpaII nlalli cauli SCLFI ncil Idsm dsaV fnuDII/mvnI bsh1236I bsh1236I hqaI aciI bstul fnuDII/mvnI bstuI mnlI aciI ahaII/bsaHI hhaI/cfoI hinl1/acy1 banI acil hinPI nlaIV hgici haeII narI kasī

FIG. 41L

CTAACATCCG CGCGGGATA TGGAACAGAC GGAGGGGCGC AACGCAGCGC CACGTACCTC GGCCCGGTGG AGCTGGACTT ACCTTCGGCC GCCGTGGAGC

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cac8I

rmaI

mael

acil

mnll caull.bfal

eco01091/drall

aviII/fspI bsiHKAI

DmyI

fnuDII/mvnI thal acil **bsh1236I** hgaI bstuI pflMI aviII/fspI hhaI/cfoI hinPI mstI ·bsmI acil

bsaJI bsli

pflMI

hphī

hinfI tfil

GATIGCCIAA GIGGIGAGGI ICTIAACCIC GGIIAGIIAA GAACGCCICI IGACACIIAC GCGIIIGGII GGGAACCGIC IIGIAIAGGI AGCGCAGGCG TCGCGTCCGC 3501 CTAACGGAIT CACCACTCCA AGAATIGGAG CCAATCAAIT CTIGCGGAGA ACTGIGAAIG CGCAAACCAA CCCTIGGCAG AACAIAICCA nlaIV pslI

haeIII/palI mscI/balI mval dsal haeI SCIFI

ecoRII

Idsm

hpall SCIFI nciI dsaV

sau96I

mboi/ndeIi[dam-]

sau3AI

nlaIV avall asuI **DPuMI**

bslI bsaJI bstNI dsaV

hinPI apyI[dcm+] sau96I avall

dpnII[dam-]

dpnI[dam+]

asul eael

bsoFI fnuDII/mvnI

fpu4HI

fnu4HI bsoFI

thaI hinPI fnu4HI

hhal/cfol hgiAl/aspHI mstI nlaIII bsp1286 nlaIV cfrI IMndd fou4BI

bsoFI bsoFI cac8I hhal/cfoI bstul

bbvI acil bsh1236I avaI bpmI/gsuI[dcm-] acil sfaNI

GGGTCCTGGC CACGGGTGCG CATGATCGTG CTCCTGTCGT TGAGGACCCG GCTAGGCTGG GTAGAGGTCG TCGGCGTGCG CCGCGTAGAG CCCGTCGCAA CCCAGGACCG GTGCCCACGC GTACTAGCAC GAGGACAGCA ACTCCTGGGC CGATCCGACC ecool091/drall msll 3601 CATCTCCAGC AGCCGCACGC GCCGCATCTC GGGCAGCGTT bbvI

fnu4HI **bsoFI** bbvI

fnu4HI **bsoFI**

fauDII/mvnI

hphī

bstul

hinfI tfil

bsrI

cac8I

thaI

3701 CGGGGTTGCC TTACTGGTTA GCAGAATGAA TCACCGATAC GCGAGCGAAC GTGAAGCGAC TGCTGCTGCA AAACGTCTGC GACCTGAGCA ACAACATGAA bbvI bsh1236I maeII

maeII

GCCCCAACGG AATGACCAAT CGTCTTACTT AGTGGCTATG CGCTCGCTTG CACTTCGCTG ACGACGACGT TTTGCAGACG CTGGACTCGT TGTTGTACTT

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sau3AI mbol/ndeII[dam-] dpnI[dam-] dpnI[dam-] dpnI[dam-] bstIl/xhoII aciI alwI[dam-] mspI mspI mpaII thaI thaI thaI thaI fnuDII/mvnI hinPI bspMII bstUI hhaI/cfoI bsaWI sfaNI bsh1236I haeII mslI accIII[dam-] fokI cac8I cackaaacGcG GaacGrGcA TTATGTTCCG GATCTGCATCC ACCTTTGCGC CTTCAGTCGC GGACGTGG CGACGATGG	foki fani 11 bsri mnli scarccata ccgccagttg trtaccctca	nlaili apoi bsli CATTAC CCCCATGAAC AGAAATTCCC
sau3AI mbol/ndeII[mamI[dam-] dpnI[dam+] dpnII[dam-] bstYI/xhoII alwI[dam-] mspI mspI hpaII mrol bsaBI[dam-] bspMII bspMII bspMII scolII[dam-] tatGTTCCG GATCTGCATC	acil bsmFI foki sau96i sfaNI nlaIV acil avaII fnu4HI asuI bsoFI TGATTTTCT CTGGTCCCGC CGCATCCATA	CGTTTCATCG GTATCATTAC GCAAAGTAGC CATAGTAATG
acil thai fnuDil/mvnl hinPl bstUl hhal/cfol bsh12361 haeIl msll CGCG GAAGTCAGCG CCCTGCACCA		mnli foki maeIII sfaNI TCAGTAACCC GTATCGTGAG CATCCTTTCATCG GTATCATTAC AGTCATTGGG CATAGTAATG
	cac8I hinPI hhal/cfoI heII ceII cGCGGCGT	
mboII bpuaI bbsI rggrctrcg ttrccgrgt rcgtaaagrc	trugi ha msel ec CCTACATCTG TATTAACGAA GGATGTAGAC ATAATTGCTT	nspl scrFI ncil mspl hpall dsaV nlallI caull maelll nspHI GTAACCGGC ATGTTCATCA
mboli bpual bbsi 1 regretrese re) CTGTGGAACA C GACACCTTGT G	bsri bsli maeli psp14061 m 11 CAACGTTCCA G

FIG. 41N



E

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED

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4101 CCTTACACGG AGGCATCAAG TGACCAAACA GGAAAAAACC GCCCTTAACA TGGCCGGCTT TATCAGAAGC CAGACATTAA CGCTTCTGGA GAAACTCAAC GGAATGTGCC TCCGTAGTTC ACTGGTTTGT CCTTTTTTGG CGGGAATTGT ACCGGGCGAA ATAGTCTTCG GTCTGTAATT GCGAAGACCT CTTTGAGTTG 4201 GAGCTGGACG CGGATGAACA GGCAGACATC TGTGAATCGC TTCACGACCA CGCTGATGAG CTTTACCGCA GCTGCCTCGC GCGTTTCGGT GATGACGGTG CTCGACCTGC GCCTACTTGT CCGTCTGTAG ACACTTAGCG AAGTGCTGGT GCGACTACTC GAAATGGCGT CGACGGAGCG CGCAAAGCCA CTACTGCCAC pbmI/gsuI[dcm-] hphI fnuDII/mvnI fnuDII/mvnI mnll bsh1236I hhai/cfoi **bsh1236I** bstul hinPI thaI bstuI thaI tru9I mseI fpu4HI acil bbvI bsoFI IIBqsu fnu4HI aluI IInad **DSOFI** bcgI bbvI aluI haeIII/palI acil bsli nlaili acil asuI mslI tru9I mseI asp700 hinfI XmbI tfiI maeIII fnuDII/mvnI sfani **bsh1236**I aluI hqaI fokI mplI acil bstul thaI

sau96I cac8I

acti 4301 AAAACCTCTG ACACATGCAG CTCCCGGAGA CGGTCACAGC TTGTCTGTAA GCGGATGCCG GGAGCAGACA AGCCCGTCAG GGCGCGTCAG CGGGTGTTGG TITIGAGAC IGIGIACGIC GAGGGCCICI GCCAGIGICG AACAGACAIT CGCCIACGG CCICGICIGI ICGGGCAGIC CCGCGCAGIC GCCCACAACC fauDII/mvaI bstUI acil hinPI nspBII bsh1236I hhaI/cfoI thaI drdI SCLFI hpall CauII nciI Idsm foki dsav sfani aciI aluI maeIII hpall Idsm caull SCIFI dsaV ncil nspHI aluI bslI fnu4BI bsoFI bbvI nlaIII Idsu

moli

bsmBI esp3I

bsmAI

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		fnu4HI bsoFI bbwI	EBB. TTT ● REFITT	maeII			sfa fnu4HT	sfani 4HT	Jobb	hgial/aspui bsp1286 bsimkal bmvT ndel
		hinPI nlaIII bsrI hhaI/cfoI tth1111,	hinPI nlaIII bsrI bsaA hhaI/cfoI tthl111/aspI	bsaAI aspI	bst aciI acc	bstl107I tru9 accI bsrI mseI	tru9I bsoFI mseI aciI	1	rsal csp6I	apali/snoi alw441/snoi
4401	CGGGTGTCGG	GGCGCAGCCA	4401 CGGGTGTCGG GGCGCAGCCA TGACCCAGTC ACGTAGCGATGT ATACTGGCTT AACTATGCGG CATCAGAGCA GATTGTACTG AGAGTGCACC GCCCACAGCC CCGCGTCGGT ACTGGGTCAG TGCATCGCTA TCGCCTCACA TATGACCGAA TTGATACGCC GTAGTCCGT CTAACATGAC TCTCACGTGG	ACGTAGCGAT TGCATCGCTA	AGCGGAGTGT TCGCCTCACA	ATACTGGCTT TATGACCGAA	AACTAIGCGG TTGAIACGCC	CATCAGAGCA (GIAGITCET)	GATTGTACTG	agagtgcacc TCTCACGTGG
						mboll earl/k sapl	mboli earl/ksp6321 apl		hinPI hhaI/cfoI	for
4501	acii ATATGCGGTG TATACGCCAC	acil TGAAATACCG (ACTTTATGGC (sfaNI hhal/cfol plei bsoFI mcri acii acii binfi bbvI bsiEI 4501 ATATGCGGTG TGAAATACC CACAGATGCG TAAGGAGAAA ATACCGCATC AGGCGCTCTT CCGCTTCCTC GCTCACTGAC TCGCTGCGCT CGGTCGTTCGT TATACGCCAC ACTTTATGC GTGTTACGC ATTCTCTTT TATGGCGTAG TCCGCGAGAA GCCGAAGGAA GCCGAAGGCAA GCCAAGGAA GCCAAAGC	TAAGGAGAAA ATTCCTCTTT	sfani acii ATACCGCATC TATGGCGTAG	hhal/cfol haell AGGCGCTCTT	acil moli ccccrrccrc	plei hinfi GCTCACTGAC T	plei bsoFi hinfi bbvi GAC TCGCTGCGCT CTG AGCGACGCGA	mcrI bsiEI CGGTCGTTCG GCCAGCAAGC
	fnu4HI bsoFI aciI fnu4HI	acii					·	nlaIII nspi	III	bslI cac8I
4601	bsofi bsr bbvi cac81 GCTGCGGCGA CGACGCCGCT	bsrBI c8I aluI GA GCGGTATCAG C' CT CGCCATAGIC GI	ICACTCAAA AGTGAGTIT	acil hinfl GGCGGTAATA CGGTTATCCA CAGAATCAGG CCGCCATTAT GCCAATAGGT	CGGTTATCCA GCCAATAGGT	tfil hinfi CAGAATCAGG GTCTTAGTCC	GGATAACGCA	DSPHI haeIII/pa aflili haei GGATAACGCA GGAAAGAACA TGTGAGCAAA AGGCCAGCAA CCTATTGCGT CCTTTCTTGT ACACTCGTTT TCCGGTCGTT	I II TGTGAGCAAA ACACTCGTTT	haell/pall hael AGGCCAGCAA TCCGGTCGTT
	scrFI mval ecoRII	thaI bstŪ	thaI fnuDII/mvnI bstUI	IVDI						

4701 AAGGCCAGGA ACCGTAAAAA GGCCGCGTTG CTGGCGTTTT TCCATAGGCT CCGCCCCCCT GACGAGCATC ACAAAAATCG ACGCTCAAGT CAGAGGTGGC TTCCGGTCTTTTAGC TGCGAGTTCA GTCTCCACCG

nlaIV

cac8I

bslI

bstNI dsaV

apyI[dcm+] haeIII/palI hael nlaIV

haeIII/palI fnu4HI bsoFI acil bsh1236I

mplI

drdI taqI

sfani

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alwNI[dcm-]

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4801 GAAACCCGAC AGGACTATAA AGATACCAGG CGTTTCCCCC TGGAAGCTCC CTCGTGCGCT CTCCTGTTCC GACCCTGCCG CTTACCGGAT ACCTGTCCGC hpall bsaWI Enu4HI Idsm **bsoFI** aciI bslI aluI mnlI hhaI/cfoI bssSI apyI[dcm+] ecoRII bsaJI bstNI dsaV apyI[dcm+] ecoRII bstNI dsaV mvaI

SCLFI

mvaI

SCIFI

CTTTGGCCTG TCCTGATATT TCTATGGTCC GCAAAGGGGG ACCTTCGAGG GAGCACGCGA GAGGACAAGG CTGGGACGGC GAATGGCCTA TGGACAGGCG

hgiAI/aspHI alw44I/snoI apaLI/snoI 4901 CTITCICCCI ICGGAAGCG IGGCGCITIC ICATAGCICA CGCIGIAGGI AICTCAGIIC GGIGIAGGIC GIICGCICCA AGCIGGGCIG IGIGCACGAA GAAAGAGGA AGCCCTTCGC ACCGCGAAAG AGTATCGAGT GCGACATCCA TAGAGTCAAG CCACATCCAG GAAGCGAGGT TCGACCCGAC ACACGTGCTT bsp1286 **bsieka**I bmyI ddeI scfI aluI hhaI/cfoI hinPI haeII

maeIII 5001 CCCCCGTIC AGCCCGACCG CIGCGCCTIA ICCGGIAACI AICGICITGA GICCAACCCG GIAAGACACG ACITAICGCC ACIGGCAGCA GCCACIGGIA GGGGGGCAAG TCGGGCTGGC GACGCGGAAT AGGCCATTGA TAGCAGAACT CAGGTTGGGC CATTCTGTGC TGAATAGCGG TGACCGTCGT CGGTGACCAT bsrI fnu4HI **bsoFI** pbvI fau4BI **bsoFI** bovi bsrI hpall Idsm SCIFI caulI dsaV ncil hinfI maeIII hhal/cfol hpall bsaWI acil hinPI fnu4HI **bsoFI** mcrI bbvI nspBII bsiEI

hha I/cfoI 5101 ACAGGATTAG CAGAGCGAGG TATGTAGGCG GTGCTACAGA GTTCTTGAAG TGGTGGCCTA ACTACGGCTA CACTAGAAGG ACAGTATTG GTATCTGCGC IGICCIAAIC GICTCGCICC ATACAICCGC CACGAIGICI CAAGAACTIC ACCACCGGAI IGAIGCCGAI GIGAICTICC IGICATAAAC CAIAGACGCG bfaI haeI scfI aciI mnlI

hinPI

rmaI maeI

haeIII/palI

bslI

FIG. 41Q

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hpall sau3AI mbol/ndell[dam-] dpnl[dam+] dpnl[dam+] aco571 bsrl aluI alwI[dam-] acil acil cac81 cTGAAG CCAGTTACCT TCGGAAAAAA AGCATTTT TTTTTTTT CAACCACCAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGA	sau3AI mboI/ndeII[dam-] hinPI sau3AI mboI/ndeII[dam-] hhaI/cfoI mboI/ndeII[dam-] dpnI[dam-] thaI dpnI[dam+] dpnI[dam+] fnuDII/mvnI dpnII[dam-] bstUI bstII/xhoII alwI[dam-] bsh1236I alwI[dam-] bstII/xhoII hgaI ddeI maeII bspHI ATTACGCGCA GAAAAAAGG ATCTCAAGAA GATCCTTTGA TCTTTTTTCTAC GGGTCTGAC GCAGTCACCT TGCTTTTTGC TAAAAACAGT TAATGCGCGC CTTTTTTTCC TAGGAAACT AGAAAAAGATG CCCCAGACTG CGAGTCACCT TGCTTTTTTCC TAAAACCAGT	sau3AI mbol/ndell[dam-] rma! hphi dpn[[dam+] mbol/ldell[dam-] sau3AI mae! tru9! mbol/ndell[dam-] msel dpn[[dam+] dpnI[[dam-] dpnI[[dam-] alw[[dam-] alw[[dam-] alw[[dam-] bstXl/xhoII bstXl/xhoII msel msel alw[[dam-] bfaI ahaIII/draI ahaIII/draI maeIII TGAGATTATC AAAAGGATC TCACCTAGA TCCTTTTAAA TTAAAAATTA AGTAAAATTA ATTTTTAAT CAATATGAG TAAAATGATA ACTCTAATAG TTTTCCTAG AAGGACA GACTGCAAT	nlaIV sau3AI hgiCI mbol/ndeII[dam-] hinfI msel mnli ddeI dpnII[dam-] fokI ahdI/eam1105I CCAATGCTTA ATCAGTGAGG CACCTATCT AGCATCTT CATTCGTT CATCCATAGT TGCCTGACT CCGTCGTAGT CTATTGCTC GGTTACGAAT TAGTCACTCC GTGGATAGAG GATAAGCAA GTAGGTATCA ACGGACTGAG GGGCAGCACA TCTATTGATG CTATGCCCTC
eco571 bsrI 5201 TCTGCTGAAG CCAG AGACGACTTC GGTC	hinPI hhal/cfoI thal fnuDII/mvnI bstUI bsh1236I 5301 ATTACGCGCA GAAA TAATGCGCGT CTTT	5401 TGAGATTATC AAAA	tru9I mseI 5501 CCAATGCTTA ATCAG GGTTACGAAT TAGT

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mstI psp1406I

tru9I

bfaI

CauII dsav

tru9I

sau96I

mseI

rmaI maeI

hpall

Idsm

ncil

SCLFI

hhaI/cfoI

hinPI

maeII

Atty Docket: GENENT.093A

nlaIII

nlaIII

dpnII[dam-] maeIII alwI[dam-]

dpnII[dam-]

mbol/ndeII[dam-]

dpnI[dam+]

aluI hpaII bsaWI Idsm

maelll

mslI sfaNI

bsoFI bbvI

hhaI/cfoI sau96I hinPI haeIII/palI 5601 GGCTTACCAT CTGGCCCCAG TGCTGCAATG ATACCGCGAG ACCCACGCTC ACCGGCTCCA GATTTATCAG CAATAAACCA GCCAGCCGGA AGGGCCGAGC CCGAAIGGIA GACCGGGGIC ACGACGIIAC IAIGGCGCTC IGGGIGCGAG IGGCCGAGGI CIAAAIAGIC GIIAIIIGGI CGGICGGCCI ICCCGGCICG asuI hpall Idsm bglI cac8I pbmI/gsuI[dcm-] cfr101/bsrFI hphI nlaIV hpaII fauDII/mvaI bsh1236I bstul thaI acil haeIII/pall bsrDI fnu4HI **bsoFI** bbvI bsrI sau96I nlaIV asuI

bsmAI

bsaI

mbol/ndeII[dam-] dpnI[dam+] aviII/fspI CGICTICACC AGGACGIIGA AAIAGGCGGA GGIAGGICAG AIAAITAACA ACGGCCCIIC GAICATIT AICAAGCGGI CAAITAICAA ACGCGIIGCA TGCGCAACGT sau3AI 5701 GCAGAAGIGG ICCIGCAACI ITAICCGCCI CCAICCAGIC IAITAAIIGI IGCCGGGAAG CIAGAGIAAG IAGIICGCCA GIIAAIAGII bsrI mseI sau3AI nlaIV aluI asel/asnl/vspl bsrI foki mnlI acil cac8I scfi pstI fnu4HI avall asuI

ACAACGGIAA CGACGICCGI AGCACCACAG IGCGAGCAGC AAACCAIACC GAAGIAAGIC GAGGCCAAGG GIFGCIAGII CCGCICAAIG IACIAGGGGG 5801 IGTIGCCAIT GCIGCAGGCA ICGIGGIGIC ACGCICGICG ITIGGIAIGG CITCAIICAG CICCGGIICC CAACGAICAA GGCGAGIIAC AFGAICCCCC bsrDI bsgI

nlaIII mslI haeIII/palI fpu4HI aciI **bsoFI** eaeI cfrI mbol/ndeII[dam-] mull dpnII(damdpnI[dam+] sau96I pvuI/bspCI sau3AI bsiEI mcrI avall asuI

Enu4HI **bsoFI** bbvI

TACAACACGT TITITCGCCA ATCGAGGAAG CCAGGAGGCT AGCAACAGTC TTCATTCAAC CGGCGTCACA ATAGTGAGTA CCAATACCGT CGTGACGTAT

5901 ATGTTGTGCA AAAAAGCGGT TAGCTCCTTC

aluI

acil

GGTCCTCCGA TCGTTGTCAG AAGTAAGTTG GCCGCAGTGT TATCACTCAT GGTTATGGCA GCACTGCATA

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hphI

hphī

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bsiEI mcrI

bcgI

fpu4HI

rsaI scal

bsrI

sfani

fokI

nlaIII

bsoFI

acil ddeI

TAAGAGAATG ACAGTACGGT AGGCATTCTA CGAAAAGACA CTGACCACTC ATGAGTTGGT TCAGTAAGAC TCTTATCACA TACGCCGCTG GCTCAACGAG ATGCGCCGAC CGAGITGCIC 6001 ATTCTCTTAC TGTCATGCCA TCCGTAAGAT GCTTTTCTGT GACTGGTGAG TACTCAACCA AGTCATTCTG AGAATAGTGT maeIII hphI csp6I

hinl1/acyI hgaI

hhaI/cfoI hinPI thaI

ahaII/bsaHI

hpall

Idsm

SCLFI

ncil dsav

mbol/ndeII[dam-]

sau3AI

dpnII[dam-] bstYI/xhoII

alwI[dam-]

Iloqu

asp700

XmbI

psp1406I

maelI

hgiAI/aspHI

bsp1286 bsiHKAI

tru9I

dpnI[dam+]

fnuDII/mvnI **bsh1236**I bstul

acil

cauli hincil/hindli

6101 TIGCCCGGCG ICAACACGCG AIAAIACCGC GCCACAIAGC AGAACTIIAA AAGIGCICAT CAIIGGAAAA CGIICIICGG GGCGAAAACI CICAAGGAIC bmyI msel

AACGGGCCGC AGTTGTGCCC TATTATGGCG CGGTGTATCG TCTTGAAATT TTCACGAGTA GTAACCTTTT GCAAGAAGCC CCGCTTTTGA GAGTTCCTAG ahaIII/draI

mpoII[dam-] eco57I sau3AI hgiAI/aspHI **bsp1286 bsiHKAI**

> mbol/ndeII[dam-] taqI

bsrI sau3AI dpnII[dam-]

dpnI[dam+]

mbol/ndeIl[dam-] dpnI[dam+] alw44I/snoI apaLI/snol bmyI

sfani

dpnII[dam-] bssSI maelli

TGAGAICCAG IICGAIGIAA CCCACICGIG CACCCAACIG AICIICAGCA ICIIIIACII ICACCAGCGI IICIGGGIGA GCAAAAACAG AATGGCGACA ACTCTAGGTC AAGCTACATT GGGTGAGCAC GTGGGTTGAC TAGAAGTCGT AGAAAATGAA AGTGGTCGCA AAGACCCACT CGTTTTTGTC alwI[dam-] bstYI/xhoII

6201 TTACCGCTGT

nspBII

aciI

fpu4BI acil

earI/ksp632I mslI **bsoFI**

TGCCGCAAAA AAGGGAATAA GGGCGACACG GAAATGTTGA ATACTCATAC TCTTCCTTTT TCAATATTAT TGAAGCATTT ATCAGGGTTA CTICCGITIT ACGCCGITIT ITCCCITAIT CCCGCIGIGC CITIACAACI IAIGAGIAIG AGAAGGAAAA AGTIAIAATA ACTICGIAAA IAGICCCAAI 6301 GAAGGCAAAA

SapI

Iloqu

RAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES Hsei et al.

Atty Docket: GENENT.093A Appl. No.: 09/234,182



hinlI/acyI maell fnuDII/mvnI

ahaII/bsaHI aatII ddeI

bstul

hinPI

thaI

bsh1236I acil

AACAGAGTAC TCGCCTATGT ATAAACTTAC ATAAATCTTT TTATTTGTTT ATCCCCAAGG CGCGTGTAAA GGGGCTTTTC ACGGTGGACT GCAGATTCTT 6401 ITGICICATG AGCGGATACA TATITGAATG TATITAGAAA AATAAACAAA TAGGGGTTCC GCGCACATIT CCCCGAAAAG TGCCACCTGA CGTCTAAGAA nlaIV hhaI/cfoI

bspHI acil bsmAI bsrBI

nlaIII rcal

haeIII/palI sau96I

Iloqu eco01091/draII asuI

bpuAI bbsI mnlI bssSI

tru9I

bapHI rcal

nlaIII

6501 ACCATTATTA TCATGACATT AACCTATAAA AATAGGCGTA TCACGAGGCC CTTTCGTCTT CAA mseI

(SEQ:1D NO.61) TGGTAATAAT AGTACTGTAA TTGGATATTT TTATCCGCAT AGTGCTCCGG GAAAGCAGAA GTT

FIG. 411

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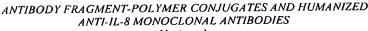
Appl. No.: 09/234,182 Atty Docket: GENENT.093A



>length: 6563

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1119 1195 1425 1434 1446 1512 1695 1696 1752 2155 2375 2727 3002 3090 3339 3463
                                                                                                                           2628 2781 2784 2787 2906 2926 3005 3045 3094 3141 3226 3241 3309 3342 3367 3412
                                                                                                                                                    3436 3448 3490 3544 3597 3613 3619 3700 3838 3967 3970 3981 4139 4155 4210 4266
                                                                                                                                                                              4351 4390 4400 4442 4467 4505 4518 4544 4561 4604 4611 4632 4723 4751 4878 4897
                                                                                                                                                                                                                                                                                                                                                                                                                                 2218 2233 2889 3292 4202 4259 4270 4319 4338 4619 4845 4935 4981 5238 5759 5859
                                                                                                                                                                                                                                                                                                                                                                                                           72 121 252 320 398 532 589 648 1126 1144 1167 1325 1386 1906 2054 2075 2126
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     412 413 712 713 1171 1471 2578 2579 3300 3870 5245 5319 5331 5416 5429 5893
                                                                                                 178 542 805 877 1340 1750 1826 2011 2039 2043 2182 2242 2384 2492 2501 2504
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     640 999 1347 1357 1449 1665 1713 1755 1764 2333 3262 3645 4705 4826 4839
                                                                                                                                                                                                          5018 5128 5263 5272 5634 5725 5916 5962 6083 6127 6204 6313 6412 6459
                                                                                                                                                                                                                                                                                                                             1645 1813 2616 2637 2751 3408 6107 6489
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 1831 4494 4992 6238
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                                                                                                                                                                                                                                                                                                                                                         5435 5454 6146
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                                                   1093 1963 4449
                                                                                                                                                                                                                                                                                                                                                                                   ahdI/eam11051(GACNNNNGTC): 346 5566
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                                                                               3867 [dam-]
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                                                                                                                                                                                                                                             see hinlI
                                                                                                                                                                                                                                                                      1307 4678
1645 6489
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  see aseI
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                         103 823
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                       5922
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  alwnI[dcm-](CAGNNNCTG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        asel/asnl/vspl(ATTAAT):
                                                                                                                                                                                                                                                                                                                                 ahall/bsaHI(GRCGYC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 alw44I/snoI(GTGCAC):
                                                                                                                                                                                                                                                                                                                                                           ahalii/drai(TTTAAA):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       apaLI/snoI(GTGCAC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             asp700(GAANNNTIC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              alwI[dam-](GGATC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            apyI[dcm+](CCWGG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       asp718 (GGTACC):
                                                                                accIII(TCCGGA):
                           acc651(GGTACC):
                                                                                                                                                                                                                                                                              aflil(ACRYGT):
aatII(GACGTC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             apaI(GGGCCC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   apol (RAATTY):
                                                       accI (GTMKAC):
                                                                                                                                                                                                                                                                                                         ageI(ACCGGT):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          asuI(GGNCC):
                                                                                                                                                                                                                                                                                                                                                                                                                    aluI(AGCT):
                                                                                                          acil(CCGC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    aspHI
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FIG. 41V



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Stop Template Primer

5' CAT GGT ATA GGT TAA ACT TAT TTA CAC 3' (SEQ ID NO.63) **SL.97.2**

NNS Randomization Primer

5' CAT GGT ATA GGT NNS ACT TAT TTA CAC 3' (SEQ ID NO.64) SL.97.3

FIG. 42

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Randomization of Position N35 of Variable Light Chain CDR-1 Amino Acid Frequency

Phage Display (NNS Codon Library) Sort #3	ay (NNS Co	don Libra	ry) Sort #3	
Amino Acid	Frequency % Total	% Total	IC50 (nM)	
Asparagine (wt)	1	5.6	4.9	
Glycine	9	16.6	3.1	
Aspartic Acid	3	16.6	3.1	
Glutamic Acid	4	22.2	0.1	
Alanine	2	5.6	0.2	
Lysine		5.6	ND	
Serine	-	1.9	ND	

FIG. 43A

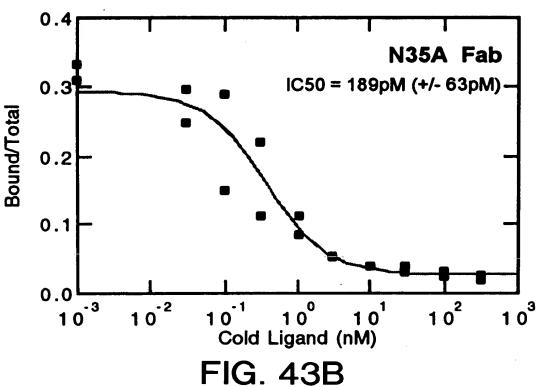


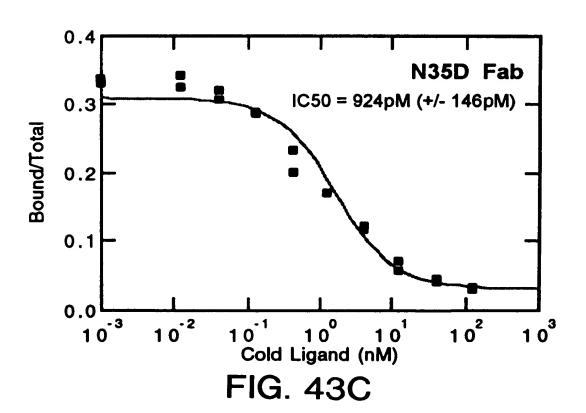
<u>.</u>;

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES

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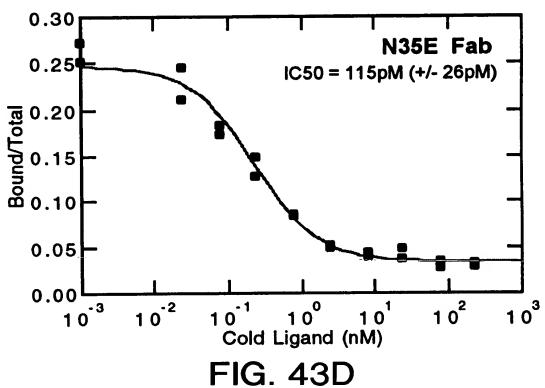
Appl. No.: 09/234,182 Atty Docket: GENENT.093A

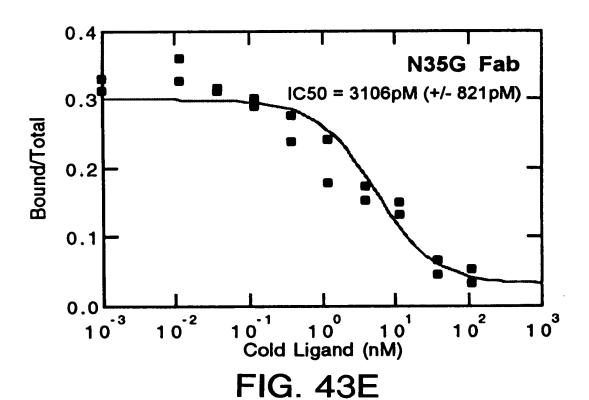




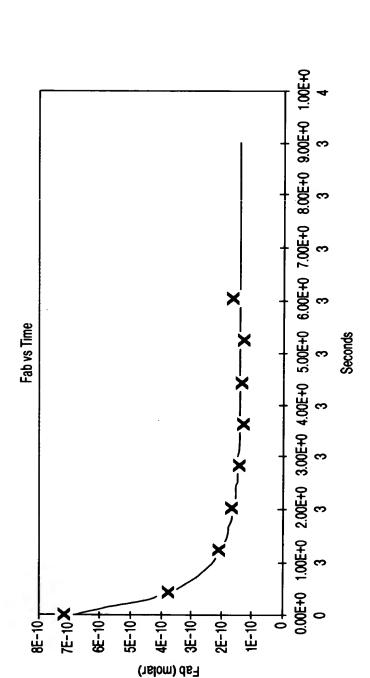
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Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.F(ab')2.

Kd	114pM	109pM	54pM
kd	Ð	$2.1x10^{-4}$	2.6x10 ⁻⁴
ka	Q	$2.0x10^6$	4.7x10 ⁶
SAMPLE	6G4V11N35A-Fab	6G4V11N35A-F(ab') ₂	6G4V11N35E-Fab

OCT 2 1 2002 ST

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES

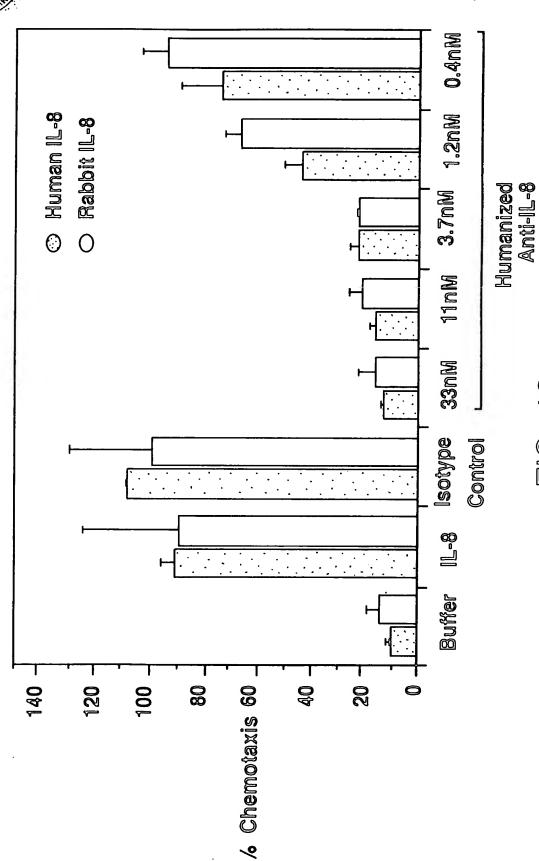
Hsei et al.
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1					TATA															
					TATA	-									AAAA F					TTTG
-23	M F		K	N	1	A	r	ь	ъ	A	5	М	F	٧	F	3	_	A	1	14
61	GCAT	CAC	:GC	ľG	TATA	CCA	GAT	GAC	CCAC	GTCC	CC	GAG	СТС	CC	TGTC	CGC	CTC	TGT	GGG	CGAT
					TATA															
-3	A)	7	Α	D	I	Q	M	T	Q	S	P	S	S	L	S	A	s	V	G	D
121					TCAC															
	TCCC	CAC	TG	ЗT	AGTG															
18	R V	7	T	I	${f T}$	С	<u>R</u>	<u>\$</u>	S	0	S	L	V	Н	G	_I_	G	E	<u>T</u>	
181					ATCA															
					TAGT															
38	L I	i	W	Y	Q	Q	K	P	G	K	A	P	K	L	L	I	Y	<u>K</u> _	<u>V</u>	_ <u>s</u>
								mmer			mai	.		~~	amma		~~~	001		0 3 0 m
241					CTGG															
					GACC'															
58	N	<u> </u>	<u>. F</u>	<u> </u>	G	V	P	S	ĸ	r	5	G	5	G	5	G	T	D	r	T
201	COC		ን አ ጣኒ	~ 7	GCAG	mcmv	-C 3	CCC	NC N	אפאר	σт.	ccc	እአሮ	יואדי	מידית	СПС	ጥጥር	ACA(ገ ልሮ	ጥልርጥ
301					CGTC.															
79					S															
70	י ע		_	3	3	ם	¥	-	خد	D	•	^	•	•	. •	_	<u> </u>		 _	
361	СУТК	יחיב	CC	3C	TCAC	بلبلئ	TGG	ACAC	GG	PACC	AAG	GGTV	GGA	GA	тсаа	ACG	AAC	TGTY	GC'	TGCA
301					AGTG															
98					T															
20	**					_		-												
421	CCA	rca	rg T	СТ	TCAT	CTT	ccc	GCC	ATC	IGAT	GA	GCA	GTT	GA	AATC	TGG	AAC	TGC	rtc'	TGTT
	GGT	\G/	ACA	GA	AGTA	GAA	GGG	CGG	rag <i>i</i>	ACTA	CT	CGT	CAA	СT	TTAG	ACC	TTG	ACG	AAG	ACAA
118	P 5	3	V	F	I	F	P	P	S	D	E	Q	L	K	S	G	T	A	S	V
						•														
481					TGAA															
		_			ACTT															
138	V	2	L	L	N	N	F	Y	P	R	E	A	K	V	Q	W	K	V	D	N
E 41	0000	~m~	70 B	N CD	CGGG	M N N	CITIC	CCN	~~ > (ግ አረተጥ	CT	~~~	202	~~	ACC A	CAG	C A A	CCN	~ A C:	CACC
541					GCCC.															
150	A I				GCCC					S								D		9199 ம
130	Α.	_	Ž	.5	G	14	3	Ā		5	•	•	_	¥		_	•		_	•
601	ТАС	AGO	ст	CA	GCAG	CAC	ССТ	GAC	зсту	GAGC	AA	AGC.	AGA	СТ	ACGA	GAA	ACA	CAA	AGTY	CTAC
002					CGTC															
178	Y									S		A			E				v	
661					TCAC															
	CGG	ACC	зст	TC	AGTG	GGT.	AGT	CCCC	GGA(CTCG		CGG	GCA	GΤ	GTTI	'CTC	GAA			
198	A (С	E	V	T	H	Q	G	L	S	S	P	V	T	K	S	F	N	R	G
																				NO.65)
721					CTGA															
					GACT		AGA	TGC	GGC	CTGC	GT.	AGC.	ACC	GG	GATC	ATG	CGT	TGA:	rca(GCAT
218	E (С	0 (SE() ID NO	.62)														

FIG. 45



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5'-CTAGTGCAGTCTGGCGGTGGCCTGGTGCAGCCAGGGGGCTCACTCCGTTTGTCCTGTGCAGCTTCTGGCTACTCCTTC-3' (SEQ ID NO.66) N35AH1upr

5'-TCGAGAAGGAGTAGCCAGAAGCTGCACAGGACAAACGGAGTGAGCCCCCTGGCTGCACCAGGCCACCGCCAGACTGCACT (SEQ ID NO.67)

N35AH1Mr

Bold indicates nucleotide change destroying Pvull site.



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>This has the pSVI backbone with the pRK7 cloning linker (pSVI7) and the intron DHFR(ID) >made from pSVI.WTSD.D by adding a linearization linker(LL) into the Hpal site > length: 8120 (circular)

cac8I

aluI

1 TICGAGCICG CCGACATIG ATTATIGACI AGAGICGAIC GACAGCIGIG GAAIGIGIGI CAGITAGGGI GIGGAAAGIC CCCAGGCICC CCAGCAGGCA AAGCICGAGC GGGCIGIAAC TAATAACIGA ICICAGCIAG CIGICGACAC CITACACACA GICAAICCCA CACCITICAG GGGICCGAGG GGICGICGI cac8I apy1[dcm+] nlaIV ecoRII BCLFI betni mvaI deav bsaJI DSmFI mbol/ndell[dam-] nspBII sau3AI aluI DVull tadI[dam-] pleI dpnII[dam-] dpnI[dam+] pvul/bspCI taqI[dam-] bsiEI ncrI hinfi bfal maeI rmaI hg1AI/aspHI ec1136II **bsp1286 DBIHKAI** hgiJII banII bmyI sacI BBtI tagi

CITCATACGI ITCGIACGIA GAGITAAICA GICGIIGGIC CACACCITIC AGGGGICCGA GGGGICGICC GICITCAIAC GITICGIACG IAGAGITAAI CAGCAACCAG GTGTGGAAAG TCCCCAGGGT CCCCAGCAGG CAGAAGTATG CAAAGCATGC ATCTCAATTA nsil/avallI nspHI cac8I Idsu sfani ppu10I nlaIII cac8I apyI[dcm+] bsmFI nlaIV ecoRII BCLFI bsaJI bstNI mval dsaV apyI[dcm+] ecoRII bstNI SCLFI dsav mvaI sexAI GAAGTATGCA AAGCATGCAT CTCAATTAGT nsil/avallI sfaNI Ppu10I nlaIII nspHI cac8I sphī Idsu 101

CCGCCCATG GCTGACTAAT TTTTTTATT acil bsaJI ncol bell deal GICAGCAACC AIAGICCCGC CCCIAACICC GCCCAICCCG CCCCIAACIC CGCCCAGIIC CGCCCAIICI acil bsrI acil acil acil fokl acil **DBMFI** 201

nlaIII

styl

FIG. 48A

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7

haeIII/palI mcri eagl/xmaIII/eclXI eael cfri bsiEI spl		5) 40
fnu4HI bsoFI	fnu4HI bsoFI rsal csp6I scfI mnlI aciI nlaIII GTACCGCCTA TAGAGGGATA AGAGGGATTTT ATCCCCGCTG CCATCATGGT CATGGCGGAT ATCTCCTAAAA TAGGGGCGAC GGTAGTACCA	real cap61 BCAI GTT CAAGTACTTC
dam-] alI GCTTTG CAAAA		/pall bsrBl acil xmnl I ddel asp700 CCGCTCA GGAACGAGTT
rmal mael styl styl bsaJl blnl avrll(dam- haell/pall stul mnll bfal mTTGGAGGCC TAGGCTT	acii rsai csp6i scfi GTACCGCCTA TAGAGCGATA AGAGGATTT CATGCCGCAT ATCTCGCTAAAA	haeII/palI haeI scrFI mvaI bsrBI ecoRII dsaV bslI bsnFI acil bslI bsmAI apy1[dcm+] taqI sfaNI bsmFI bsnFI bsaJI mnli ddeI 501 TCGACCATTG AACTGCATCG TCGCCGTGTC CCAAAATATG GGGATTGGCA AGAACGGAGA CCTACCCTCG CCTCCGCTCA AGCTGGTAAC TTGACGTAGC AGCGGCACAG GGTTTTATAAC CCCTAACCGT TCTTGCCTCT GGATGGGACC GGAGGCGAGT
mnli bseRI TG AGGAGGCTTT '		bsmal bsal ca agaacgaga (
NTCC AGAAGTAG	maeII maeIII CAAG AGTGACGTAA GTTC TCACTGCATT	TATG GGGATTGGC
lI ddel [mnll aluI haeIII/pall ccccrcr GacT7	tfil hinfl acil thal fnuDII/mvnI bstUI bsh12361 CGCGGATTCC CCGTGCCAAG	pflMI bslI. bsmFl ccgrgrc ccaaaatarg
fnu4HI bsoFI bglI sf1I haeIII/palI haeIII/palI bsaJI mnlI bsaJI acil h GAGG CCGAGGCCGC CTCG	scrfi ncii nsi hpali thai dsav cauli CCGGAACG TGCATTGGAA CGCG	taqI sfaNI bsmF TCGACCATTG AACTGCATCG TCGCCGTGTC AGCTGGTAAC TTGACGTAGC AGCGGCACAG
ha mnli 301 TATGCAGAGG ATACGTCTCC	scrFI nciI mspI hpaII dsaV cauII 401 CCGGGAACGG	taqi 501 TCGACCATTG AGCTGGTAAC

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tru9I mseI ahaIII/draI	CCTTTAA GGAAATT			ı	I TTATTGA AATAACT
tfil hinfi ddeI mboll tagI	TGAGAAGAAT CGA ACTCTTCTTA GCT			tru9I	aflii/bfri foki sfani msei GGAT GATGCCTTAA GACT CCTA CTACGGAATT CTGA
cm+	T TCTCCATTCC A AGAGGTAAGG				XI foki A AAGTTTGGAT T TTCAAACCTA
scrFI mvaI ecoRII dsaV bstNI apyI[dcm+]	GG AAAACCTGG CC TTTTGGACC		spHI I		bstXI TT TTCTTGCCAA AA AAGAACGGTT
	AT TATGGGTA TA ATACCCAT	sst. saci hqiJII	hgiAI/aspHI ecll36II bsp1286	bsinkai bmyi mnli alui	bssSI banII bseRI cACGA GGAGCTCA
tfiI hinfI hphI alwNI [dcm-]	CAAAGAATGA CCACAACCTC TTCAGTGGAA GGTAAACAGA ATCTGGTGAT TATGGGTAGG AAAACCTGGT TCTCCATTCC TGAGAAGAAT CGACCTTTAA GTTTCTTACT GGTGTTGGAG AAGTCACCTT CCATTTGTCT TAGACCACTA ATACCCATCC TTTTGGACCA AGAGGTAAGG ACTCTTCTTA GCTGGAAATT				msel ddel aflil/bfri asel/asnl/vspl AGGACAGAAT TAATATAGTT CTCAGTAGAG AACTCACAAGA ACCACCACGA GGAGCTCATT TTCTTGCCAA AAGTTTGGAT GATGCCTTAA GACTTATTGA TCCTGTCTTA ATTATATCAA GAGTCATCTC TTGAGTTTCT TGGTGGTGCT CCTCGAGTAA AAGAACGGTT TTCAAACCTA CTACGGAATT CTGAATAACT
eco571 mboI1 earl/ksp6321 mn1	CTC TTCAGTGGAA SAG AAGTCACCTT				ddeI vspI GTT CTCAGTAGAG CAA GAGTCATCTC
* iu	601 CAAAGAATGA CCACAACCTC TTCAGTGGAA GGTAAACAGA ATCTGGTGAT TATGGGTAGG AAAACCTGGT TCTCCATTCC TGAGAAGAAT CGACCTTTAA GTTTCTTACT GGTGTTGGAG AAGTCACCTT CCATTTGTCT TAGACCACTA ATACCCATCC TTTTGGACCA AGAGGTAAGG ACTCTTCTTA GCTGGAAATT			tru9I	msel ddel afli/bfri asel/asni/vspi 701 aggacagaar taatatagat ctcagtagag aactcaaaga accaccacga ggagctcatt ttcttgccaa aagtttggat gatgccttaa gacttattga rcctgtctta attatatcaa gagtcatctc ttgagtttct tggtggtgct cctcgagtaa aagaacggtt ttcaaaccta ctacggaatt ctgaataact

FIG. 48C

801 ACAACCGGAA TIGGCAAGIA AAGIAGACAI GGITIGGAIA GICGGAGGCA GTICIGITIA CCAGGAAGCC AIGAAICAAC CAGGCCACCI TAGACICITI IGIIGGCCII AACCGIICAI IICAICIGIA CCAAACCIAI CAGCCICCGI CAAGACAAAI GGICCIICGG IACIIAGIIG GICCGGIGGA AICIGAGAAA

accI nlaIII

mspI hpaII bsaWI

hinfI ddel plei

hinfi apyl[dcm+] betNI

ecoRII

ecoRII

mvaI

dsaV

tfil

nlall

bstNI dsav

apyI[dcm+]

SCLFI

haeIII/palI haeI

mnlI

I I oqu

Iloqu

sfaNI

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ahaII/bsaHI hinli/acyi hgal

mnll SCLFI mvaI

ecoRII

bstNI dsav

ecoNI apyI[dcm+] bsaJI

mnlI

ball ddel

mn]I

901 GTGACAAGGA TCATGCAGGA ATTTGAAAGT GACACGTTTT TCCCAGAAAT TGATTTGGGG AAATATAAAC CTCTCCCAGA ATACCCAGGC GTCCTCTC CACTGTTCCT AGTACGTCCT TAAACTTTCA CTGTGCAAAA AGGGTCTTTA ACTAAACCCC TTTATATTTG GAGAGGGTCT TATGGGTCCG CAGGAGAC

afllII

mbol/ndeII[dam-]

nlaIII

maellI

apoI

maeIII alwI[dam-]

dpnII[dam-]

dpnI[dam+]

CORII bstNI dsaV mvaI

SCLFI

apyI[dcm+]

sau96I

avall

mnll

accI sfaNI asuI

1001 AGGTCCAGGA GGAAAAAGGC ATCAAGTATA AGTTTGAAGT CTACGAGAAG AAAGACTAAC AGGAAGATGC TTTCAAGTTC TCTGCTCCCC TCCTAAAGCT TCCAGGTCCT CCTTTTCCG TAGTTCATAT TCAAACTTCA GATGCTCTTC TTTCTGATTG TCCTTCTACG AAAGTTCAAG AGACGAGGGG AGGATTTCGA *END DHFR

bsaJI sau3AI

mbol/ndeII[dam-] dpnII[dam-] dpnI[dam+]

nlaIII

styl ncol

alwI[dam-] bstYI/xhoII

cacel dsal bsmFI

nsil/avallI

ppu10I

asel/asnl/vspl

tru9I mseI

fnu4HI

bsoFI

bbvI

1101 ATGCATTITI ATAAGACCAT GGGACTTTTG CTGGCTTTAG ATCCCCTTGG CTTCGTTAGA ACGCAGCTAC AATTAATACA TAACCTTATG TATCATACAC TACGTAAAAA TATTCTGGTA CCCTGAAAAC GACCGAAATC TAGGGGAACC GAAGCAATCT TGCGTCGATG TTAATTATGT ATTGGAATAC ATAGTATGTG bsaJI

sau96I avall asuI

ecoRII SCIFI mval

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apol

ecoRI tadī clal/bsp106

hspDI[dam-]

bsaJI

apyI[dcm+]

bell beaJI

fokī

hphI scfI

1201 ATACGATTTA

maeIII

bstNI dsav

mval fnu4HI

scrFI

ecoRII

dsaV

rmaI maeI bfaI

haeI

bpmI/gsul[dcm-]

rmaI maeI

ball fokl

nlaIII

pflMI

ncol dsaI

styl

TATGCTAAAT CCACTGTGAT ATCTATTGTA GGTGAAACGG AAAGAGGGGT GTCCACAGGT GAGGGTCCAG GTTGACGTGG AGCCAAGATA GCTAACTTAA

seq from pRK6G425VH: Cla-AvrII^

GGTGACACTA TAGATAACAT CCACTITGCC TITCTCTCCA CAGGTGTCCA CTCCCAGGTC CAACTGCACC TCGGTTCTAT CGATTGAATT

bstNI bsoFI apyI[dcm+] bbvI

eco01091/drall GCCAGGGGGC TCACTCCGTT TGTCCTGTGC AGCTTCTGGC TACTCCTTCT CGAGTCACTA TATGCACTGG GTCCGTCAGG CCCCGGGTAA GGGCCTGGAA CAGGCAGTCC GGGGCCCATT CCCGGACCTT GGTGGTACCC TACCAGTACA TAGTAGGAAA AAGATCATCG TTGACGTTGA CCTCATGTAA GTCTTCAAGT GGATCACGTC AGACCGCCAC CGGACCACGT TICTAGIAGC AACTGCAACT GGAGTACATI CAGAAGIICA GCTAGIGCAG ICIGGCGGIG GCCIGGIGCA acil haeIII/palI ecoRII scrFI dsaV mvaI bslI apyI[dcm+] haeIII/pall sau96I eco01091/drall asul bstNI xmaI/pspAI haeIII/palI <u>ပ</u> G caull hpall SCIFI dsaV asul bell Idsm scrFI ncil caull bsaJI smal ncil dsaV bslI bsaJI ۵, ه 0 avaI sau961 nlaIV > œ nlaïv asuI aluI ATACGTGACC sau96I о > berI avall Σ CGGTCCCCCG AGTGAGGCAA ACAGGACACG TCGAAGACCG ATGAGGAAGA GCTCAGTGAT SHY aval maelll csp6I pleI paeR7I xhoI bsrI hinfI tagI bfaI alwNI[dcm-] fnu4HI **bsoFI** bbvI 1301 CCACCATGGG ATGGTCATGT ATCATCCTTT **ب** ن aluI nlalli foki L R **bep1286** hgiJII mval banII apyI[dcm+] bmyI bsaJI ecoRII ပ BCLFI bsaJI batNI daav ρ,

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thai haelil/pall bstUl hau961	mil bmyl zaccerc rccaagaca srgggagg aggirercgr P S K S T
ATAATCAAAA GTTCAAG IATTAGTTTT CAAGTTC N Q K F K mnl CTATTACTGT GCAAGAG GATAATGACA CGTTCTC Y Y C A R G Sau961 a1V iJII mboli ecoRii a1 bpuAi haelii/pali asu1 bbsi	TCTTCCC
bell sau3Al mbol/ndell[dam-] dpnl[dam+] alw1[dam-] alw1[dam-] alw1[dam-] bp S N G E T T Y D P S N G E T T Y Cac8	mAI haeIII/pall ecol091/draII TCTCCTCGC CTCCACCAG GGCCCATCGG AGAGGAGCC GAGGTGTTC CCGGTAGCC S S A S T K G P S V
bell sau3AI mbol/ndell dpnI[dam+] dpnI[dam+] dpnI[dam-] 01 TGGGTTGGAT ATATTGATCC TTCCl ACCCAACCTA TATAACTAGG AAGG; 47 W V G Y I D P S P scfl bsgl cac8I bspMI cac8I cac8I bspMI cac8I cac8I cac8I bspMI cac8I cac8I cac8I cac8I bspMI cac8I cac8I cac8I bspMI cac8I cac8I bspMI cac8I cac8I bspMI cac8I cac8I bspMI acreCTGCACG GCACG RI ACTGCCGCAC GCACG RI ACTGCCGAC GCACG RI ACTGCCACG GCACG RI ACTGCACG GCACG RI ACTGCCACG GCACG RI ACTGCA	nlary battering by tropaggaacc creditational action and action of the control of
1501 47 1601 81	1701

FIG. 48F

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ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES

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ahdI/eam1105I

sau96I

avall

SCFFI

asuI

mvaI

1801 CTGGGCTGCC TGGTCAAGGA CTACTTCCCC GAACCGGTGA CGGTGTCGTG GAACTCAGGC GCCCTGACCA GCGGCGTGCA CACCTTCCCG GCTGTCTAC GACCCGACGG ACCAGITCCI GAIGAAGGGG CIIGGCCACI GCCACAGCAC CIIGAGICCG CGGGACIGGI CGCCGCACGI GIGGAAGGGC CGACAGGAIG hpall ddel hhal/cfol nspBII alw441/snol cauII Idsm SCLFI ncil dsav T F P acil apaLI/snoI **bsp1286** hgiAI/aspHI G V H DmyI cac8I **beiHKAI** fnu4HI **bsoFI** တ A L ahaII/bsaHI hinl1/acyI hinPI hgici haeII narI banI S S nlaIV kası ageI tthllll/aspI cfr101/bsrFI E P V T hphI hpall Idsm bsaWI maeIII bsll <u>ч</u> V K apyI[dcm+] ecoRII ecoNI bstNI mvaI dsav bslI I G C L fnu4HI bsoFI bbvI 147

BCLFI

1901 AGTCCTCAGG ACTCTACTCC CTCAGCAGCG TGGTGACTGT GCCCTCTAGC AGCTTGGGCA CCCAGACCTA CATCTGCAAC GTGAATCACA AGCCCAGCAA TCAGGAGTCC TGAGATGAGG GAGTCGTCGC ACCACTGACA CGGGAGATCG TCGAACCCGT GGGTCTGGAT GTAGACGTTG CACTTAGTGT TCGGGTCGTT hinfi maeII z U bfal alui bsp1286 nlaIV hgici banI bmyI bsoFI hphi bmyi mnli bbvi rmaI bsp1286 maeI P S Λ Τ Λ maeIII fnu4HI bsoFI mnll bbvI bsu361/mstII/sauI ddeI mnll hinfI ddeI pleI eco811

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fnu4HI

bbsI mnlI 2001 CACCAAGGIG GACAAGAAAG TIGAGCCCAA ATCTIGIAC AAAACTCACA CAIGCCCACC GIGCCCAGCA CCTGAACTCC IGGGGGGACC GICAGTCTIC GIGGTICITIC AACTCGGGII TAGAACACTG TITIGAGIGI GIACGGGIGG CACGGGICGI GGACTIGAGG ACCCCCCTGG CAGICAAGA bpuAI DSmFI apyI[dcm+] bsaJI ecoRII bstNI dsav bmyI alwNI[dcm-] CPA bsp1286 nlaIII nspHI Idsu KTHT maeIII တ E P X **bsp1286** hgiJII banll bmyI T K V bsaJI

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		drdi mnli mboli ddel bpuAl eco811 bbsI bsu361/mstII/sauI cGAAGACCCT GAGGTCAAGT GCTTCTGGGA CTCCAGTTCA		acil fnu4HI mnll rsal maell bsoFl bseRI csp61 bsoFl bseRI csp61 bsaAI GACAAAGCCG CGGGAGGAGC AGTACAACAG CACGTACCGT GTGGTCAGCG TCCTCACGT CTGTTTCGGC GCCTCCTCG TCATGTTGTC GTGCATGGCA CACCAGTCGC AGGAGTGGCA T K P R E E Q Y N S T Y R V S V L T V
		meeII ACGTGAGCCA TGCACTCGGT V S H	rsal	csp6I maeII bsaAI CACGTACCGT GTGCATGGCA I Y R
		11 Gregregres Grecaccacc	3	rsal csp61 c agracacag c tcatgregc p y n s
sau96I nlaTV	I	avali nlaili [[dam-] nspl [I mnli nspHI] ddel msli n-] eco8li maelli asul bsu361/mstli/saul GGACCCTGA GGTCACATGC CCTGGGGACT CCAGTGTACG T P E V I C	acil thal fnuDII/mvnI bstUI bsh12361 sacil/sstII nspBII kspI dsaI bsaJI	acil fnu4HI mnll bsoFI bseRI ACAAAGCCG CGGGAGGAGGTGTTTCGC GCCCTCCTCCTCTTTTTTTTTT
v	mspI hpall scrFI nclI dsaV	sau3AI avaII mbol/ndeII[dam-] nlaIII cauII rcaI dpnI[dam+] d mnlI dpnII[dam-] ec ACACCCTC ATGATCTCCC GGACCCC FGTGGGAG TACTAGAGG CCTGGGG T L M I S R T P		mnli SGAGGTGC ATAATGCCAA G SCTCCACG TATTACGGTT C E V H N A K
		sau3Al avaII niaili mbol/ndeII[dam-] nspl nlaII cauII mnli nspHi rcal dpnI[dam+] ddeI msli earl/ksp6321 bsaJi msli bspHI[dam-] eco811 maeIII earl/ksp6321 bsaJi msli bspHI[dam-] asuI bsu361/mstII/sauI maeII bbsI bsu361/mstII/s GAGAAGCCCC CAAAACCCA GGACCCCTC ATGATCTCCC GGACCCCTGA GGTCACATGC GTGGTGGTGG ACTCAGCCA CGAAGACCCT GAGGTCAAGT GAGAAGGGGG GTTTGGGTT CCTGTGGGAG TACTAGAGGG CCTGGGGACT CCAGTTGC GACCACCACC TGCACTCGGA CTCCAGTTCA GAGAAGGGGG GTTTTGGGTT CCTGTGGGAG TACTAGAGGG CCTGGGGACT CCAGTTGAGG CACCACCACC TGCACTCGGA CTCCAGTTCA A N I S R T P E V T C V V D V S H E D P E V K F	maeli	csp61 csp61 bsrl bsaAl 2201 TCAACTGGTA CGGGACGCC GTGGAGGTGC ATAATGCCAA GACAAAGCCG CGGGAGGAGC AGTACAACAG AGTTGACCAT GCACCCG CACCTCCACG TATTACGGTT CTGTTTCGGC GCCCTCCTCG TCATGTTGTC 281 N W Y V D G V E V H N A K T K P R E E Q Y N S

bsoFI bbvI DSII apyl[dcm+]
2301 CCTGCACCAG GACTGGCTGA ATGGCAAGGA GTACAAGGTG AAGGTCTCCA ACAAAGCCCT CCCAGCCCCC ATCGAGAAAA CCATCTCCAA AGCCAAAGGG
GGACGTGGTC CTGACCGACT TACCGTTCCT CATGTTCACG TTCCAGAGGT TGTTTCGGGA GGGTCGGGG TAGCTCTTT GGTAGAGGT TCGTTTCCC
314 T. H O D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G fnu4HI bsmAI rsal ecoNI bstNI bsrI ecoRII dsav

scrFI

FIG. 48H

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED

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ncil

nlalv mboli scfl cac8I 2401 CAGCCCCGAG AACCACAGGT GTACACCCTG CCCCCATCCC GGGAAGAGAT GACCAAGAAC CAGGTCAGCC TGACCTGCCT GGTCAAAGGC TTCTATCCCA 2501 GCGACATCGC CGTGGAGTGG GAGAGCAATG GGCAGCCGGA GAACAACTAC AAGACCACGC CTCCCGTGCT GGACTCCGAC GGCTCCTTCT TCCTCAAG CITCITGATG ITCIGGIGGG GAGGGCACGA CCIGAGGCIG CCGAGGAAGA AGGAGAIGIC GTCGGGGCTC TIGGIGICCA CAIGIGGGAC GGGGGIAGGG CCCTICICIA CIGGIICIIG GICCAGICGG ACIGGACGGA CCAGIIICCG AAGAIAGGGI × > apyl[dcm+] bstNI ecoRII bspMI hinfi BCrFI dsav apyI[dcm+] nlallI ecoRII ppu10I SCFFI sexAI batNI deav mvaI mnlI earI/ksp632I E E N bsaJI mboII xmal/pspAI II oqu bpuAI hpall cauli dsav Idsm cauli bsp14071/bsrGI bslI avaI SCLFI dsav smaI ncil CICICGIIAC CCGICGGCCI P S R hpaII O P E Idsm fokI fnu4HI bsoFI bslI bbvI S bsrDI Y T csp6I CGCTGTAGCG GCACCTCACC > E mell beaJI dsaI bslI

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GITCGAGIGG CACCIGITCI CGICCACCGI CGICCCCIIG CAGAAGAGIA CGAGGCACIA CGIACICCGA GACGIGIIGG IGAIGIGCGI CIICICGGAG

z U

V D K

X L T

2601 CAAGCTCACC GTGGACAAGA GCAGGTGGCA GCAGGGGAAC GTCTTCTCAT GCTCCGTGAT GCATGAGGCT CTGCACAACC ACTACACGCA

nlaIII

xmnI bbsI

maelI

fnu4HI **bsoFI**

asp700

Lydd IMqsd

aluI bsaJI

dsaI hphI

earI/ksp632I

mboll mull sapI

> nsil/avalll sfaNI mull

GAAGAGCCTC

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sau96I

nlaIII alwI[dam-] 2801 AATAAAGCAA TAGCATCACA AATTTCACAA ATAAAGCATT TTTTTCACTG CATTCTAGTT GTGGTTTGTC CAAACTCATC AATGTATCTT ATCATGTCTG TGCAGCTTAT AATGGTTACA agggacagag gcccatttac tcacgctgcc gggatctcag ctggacgtct tcgaaccggc ggtaccgggt tgaacaaata acgtcgaata ttaccaatgt s l s p g k o (SEQ ID NO 11) ttatttegtt atcgtagtgt ttaaagtgtt tatttegtaa aaaaagtgae gtaagateaa caceaaeag gtttgagtag ttacatagaa tagtacagae maeIII aluI fnu4HI bsoFI bbvI 2701 TCCCTGTCTC CGGGTAAATG AGTGCGACGG CCCTAGAGTC GACCTGCAGA AGCTTGGCCG CCATGGCCCA ACTTGTTTAT haeIII/pall rsaI asuI bsoFI nlaIII aluI haeIII/palI hindili bqll bsaJi dsaI ncol styl fnu4HI acil sfil cfrI eaeI maeI bfal DemI mael hincil/hindil pstI begI asul bfal acci bspMI tagi rmal sall sau96I hinfI pleI haeIII/pall sfaNI apol mbol/ndeII[dam-] dpnII[dam-] hpall BCLFI Caull dpnI[dam+] dsav ncil Idsm pvuI/bspCI SISP **DSMAI** sau3AI **b**siei mcrl belI 447

FIG. 48J

GATCGATCGG GAATTAATTC GGCGCAGCAC CATGGCCTGA AATAACCTCT GAAAGAGGAA CTTGGTTAGG TACCTTCTGA GGCGGAAAGA ACCATCTGTG CTAGCTAGCC CTTAATTAAG CCGCGTCGTG GTACCGGACT TTATTGGAGA CTTTCTCCTT GAACCAATCC ATGGAAGACT CCGCCTTTCT TGGTAGACAC

mnli ddel acil

asp718

acc651

mnlI

mnlI

dsal haeIII/palI

haeI

fnu4HI

tagl[dam-] tru9I
clai/bspl06[dam-]
bspDI[dam-] mseI

bsoFI styI

bbvI hinPI

XanI

sau3AI

hhal/cfol nlalli

bsaJI

dpnII[dam-] ase1/asnI/vspI

2901

mbol/ndeII[dam-]
dpnI[dam+] asp700

csp6I

nlaIV

kpnI hgiCI

banI

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ppul01 ppul01 mvaI mvaI mvaI mvaI mvaI mvaI mvaI mvaI	sfaNI ppul01 nsil/avaIII laIII hh nspl nspli cac81 CAAAGCATGC ATCTCAATTA GTCAGCAACC ATAGTCCCGC CCCTAACTCC GCCCTAACTC GTTTCGTACG TAGAGTTAAT CAGTCGTTGG TATCAGGCG GGGATTGAG	fnu4HI bsoFI bglI sfil malI/palI malI mnli aluI mnli mnli bsaJI acil haeIII/palI mnl bsaJI acil haeIII/palI mnlAalI bsaJI acil bsaJI acil bsaJI cGACTGACTAAT TTTTTTTTTT TATGCAGAGG CCGAGGCCGC CTCGGCCTT GACTATTC AGAAGTAGTG
sfaNI ppul0I nsil/avallI nlallI sphI nsplI nspHI cac8I cac8I TTCATACGT TTCGTACGTA GA	acil bsmFi sTCAGCAACC ATAGTCCCGC CC	fnu4HI bsoFI bglI sfli haeIII/palI mnlI mnlI ddeI mnlI bsaJI acil haeIII/palI mnlCGGGCGC CTCGGCCTCT GAGCT ATACGTCTCC GGCTCCGGG GAGCCGGAGA CTCGA
## SCIFI ### SCIFI #### SCIFI ###################################	nlalv scrFI mval mval ecoRII dsaV bstNI apyI[dcm+] bsaJI cac8I cac8I AGGGTCCGC CCCTAACTC GTTTCGTAC TAGACTTAAT CAGTCGTTGG TATCAGGCG GGGATTGAG acific cacgaractac caccaractac ca	fnu4HI bsoFI bsoFI bsli styl ncol bslI dsal bsrI acil baajl 3201 CGCCCAGTTC CGCCCATCT CGCCCATC GACTGATTC AGAAGTAGTG GCGGTCAAG GCGGGGTAAG GTTTTTTTTTTTTTTTTTT
3001 GAATGTGTGT CAGTTAGGGT	nlalv scrfl mval ecoRII dsav bstNI apyl[dcm+] bsaJI cac8I 3101 TCCCCAGGCT CCCCAGCAGG AGGGTCCGA GGGTCGTCC GTCTTCATAC	bsrI acil acil cecccatrer cececatrer cececatras

FIG. 48K

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES Hsei et al. Appl. No.: 09/234,182 Atty Docket: GENENT.093A



		uDII/mvnI tUI h12361 cGGATTCC CCGTGCCAAG·AGTCAGGTAA GCCTAAGG GGCACGGTTC TCAGTCCATT Ul matched splice donar^	sau3AI mboI/ndeII[dam-] dpnI[dam+] dpnII[dam-]
	tfii hinfi acii thai	fnuDII/mvnI bstUI bsh1236I cGCGGATTCC CCG GCGCCTAAGG GGC	sau mbo dpn dpn alw
	eclXI	SG TGCATTGGAA CC ACGTAACCTT	
scrFI ncil mspI hpaII dsaV haeIII/palI	E 0 0 0	nhel bsiEI cac8I mspI caulI aluI hpaII SGCTTTTG CAAAAAGCTA GCTTATCCGG CCGGGAACGC CCGAAAAC GTTTTTCGAT CGAATAGGCC GGCCCTTGCC icom pSVI6B5-6G4VL: AvrII - HindIII frag	
	aluI rmaI maeI bfaI	nheI cac8I aluI CAAAAAGCTA GC GTTTTTCGAT CG	
rmal mael styl	bsaJI blnI avrII[dam-] haeIII/palI	stul nhel bsiEl fnuDII/mvnI hael cac81 mspl cauli bstUI mnll bfaI alu! hpall 3301 AGGAGGCTTT TTTGGAGGCC TAGGCTTTTG CAAAAAGCTA GCTTATCCGG CCGGGAACGG TGCATTGGAA CCGGGATTCC CCGTGCCAAG AGTCAGGTAA TCCTCCGAAA AAACCTCCGG ATCCGAAAAC GTTTTTCGAT CGAATAGGCC GGCCCTTGCC ACGTAACCTT GCGCAAAGG GGCACGGTTC TCAGTCCATT **Seq from pSV16B5-6G4VL: AvrII - HindIII frag Ul matched splice donar*	
		mnll AGGAGGCTTT TCCTCCGAAA	
		3301	

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	u-]						fo	ACACTGACA	TGTGACTGT		tch	, a
taqI[dam-]	clal/bsp106[dam-]	bspDI[dam-]		mbol/ndeII[dam-]	am+]	dam-)	. [-u	ATCCTACTG	TAGGATGAC	ATG	^U2 match	lariat consensus^
tagi	cla1/	Idqad	sau3AI	m/lodm	dpnI[dam+]	dpnii	alwI [da	TTTTGGATC G	TCCGGGTGGG GGAACCGAAG CAATCTTGCG CCGATGTTAA TTATGTATTG GAAAACCTAG CTAGGATGAC TGTGACTGTA	^removed ATG		lari
					H		asnI/vspI	ATACATAAC C	TATGTATTG G			
					I tru9	mseI	aseI/	AATT A	TTAA T			
	fnu4HI	bsoFI	1	.	fnuDII/mvnI tru9I	H	1236I	GGCTAC	CCGATG	L		
	for	peq	acil	thaI	funj	bst	Dsh.	GTTAGAACGC	CAATCTTGCG	^sp6 promoter		
					tyl		BaJI	CTTGGCTTC	GAACCGAAG	8,		
				bstXI	sau961 s	haeIII/palI	asuI bsaJI	SGCCCACCC C	SCGGGTGGG G			
					scfI	plei	csp61 scfl hinfl asul bsaJI bsh12361 asel/asn1/vsp1 alw1[dam-] fok1	AGAGTCTAT A	TCTCAGATA T			
					acil	saI	sp6I scfI	TACCGCCTA TA	LATGGCGGAT ATCTCAGATA			
						Ĥ	Ü	10	ਹ ਹ			

3401

lariat consensus^ IgG vH natural lariat restored^

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rmaI

sau96I avall asul

nlalii	styl	pflMI	ncol	ecoRI dsaI		m-] beaJI	GAATTC CACCATGGGA	GETGAAAAG AAAAAGAGGI GICCACAGGI GAGGGICCAG GIIGACGIGG AGCCAAGCGC IICGAICGAA CCCGACGIAG CIAACIIAAG GIGGIACCCI										
		clal/bsp106	sfani	fnu4HI	bsofi taqi apol	bbvI bspDI[da	GGCTGCATC GATT	CCCGACGTAG CTAA		aluI	sstI	sacī	hgiJII	hgiAI/aspHI	ecl136II	bsp1286	DSIHKAI	
maeI	bfaI	thal nhel	fnuDII/mvnI	bstUI cac8I	bsh1236I aluI	nruI aluI	GTTCGCG AAGCTAGCTI	CAAGCGC TTCGATCGA	cloning linker									
			Inuj		cm+] mnlI	bsaJI	C CAACTGCACC TCGC	G GTTGACGTGG AGC	^clonir									
SCLFI	mvaI	ecoRII	dsav	bstNI	apyI [dcm+]	bell beali	TGTCCA CTCCCAGGI	ACAGGT GAGGGTCCA										
							TTTTTCTCCA CAGG	AAAAAGAGGT GTCC										
							3501 CCACTTTTC	GGTGAAAAG										

		TCTAGTAGCA ACTGCAACTG GAGTACATTC AGATATCCAG ATGACCCAGT CCCCGAGCTC CCTGTCCGCC TCTGTGGGCG AGATCATCGT TGACGTTGAC CTCATGTAAG TCTATAGGTC TACTGGGTCA GGGGCTCGAG GGACAGGCGG AGACACCCGC	DIQ MIQS PSS LSA SVGD					H		AGGTCAAGTC AAAGCTTAGT ACATGGTATA GGTGCTACGT ATTTACACTG GTATCAACAG AAACCAGGAA AAGCTCCGAA	TCCAGTTCAG TTTCGAATCA TGTACCATAT CCACGATGCA TAAATGTGAC CATAGTTGTC TTTGGTCCTT TTCGAGGCTT	RSSOSLV HGIGATY LHW YQO KPGKAPK
٠	-	TCTG	> s					bstNI aluI	apyI[dcm+]	AAGC	TTCG	æ
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		GAC	i i	60	E	a	D	Д	Ø	AAC	TTG	Δ.
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bemfi bmyi	a asp	8 8								GI	S	×
gq ,	bsrl aval tthllll/aspl banll	PAGI	ຜ ~						bsrI	CTG	GAC	3
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	Ţ	ATG	Σ							ATT	TAA	Н
		STC	~				maeII	snaBI	bsaAI	GI	SCA	×
	Κζ	ATCC TAGG	_				Ĕ	Sna	per	CIA	GAT(E
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rsaI	suI	GTA							laI	ATG	TAC	
	bpm1/gsu1[dcm-] bsr1 csp6I	2 2				rsaI		aluI csp6I	hindiii nlaiii	r AC	T T	144
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		CTT		80	þ8	pg	88 e	bspMI	н	Ę	GGA	0
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	nlaIII fokI	IGGICAIGIA ICAICCITIT ACCAGIACAI AGIAGGAAA					hphI	maeIII	batEII	TCA	AGT	H
	n l	TCA						=	Þ	1666	ည	**
		TGG ACC								AT	TAT	18 R V T I T C
		3601 TGGTCATGTA TCATCCTTTT ACCAGTACAT AGTAGGAAAA	-							3701 ATAGGGTCAC CATCACCTGC		18
		က								m		



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ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED Hsei et al.

Atty Docket: GENENT.093A Appl. No.: 09/234,182

fnu4HI haeIII/palI bsoFI bbvI mbol/ndeII[dam-] fnu4HI scfI pstI bsgI **b**soFI 3801 ACTACTGATT TACAAAGTAT CCAATCGATT CTCTGGAGTC CCTTCTCGCT TCTCTGGATC CGGTTCTGGG ACGGATTTCA CTCTGACCAT CAGCAGTCTG bbvI GTOGGTCTTC TGAAGCGTTG AATAATGACA AGTGTCTCAT GAGTACAGGG CGAGTGCAAA CCTGTCCCAT GGTTCCACCT CTAGTTTGCT TGACACCGAC TVAAA GATCAAACGA ACTGTGGCTG 4001 CACCATCTGT CTTCATCTTC CCGCCATCTG ATGAGCAGTT GAAATCTGGA ACTGCTTCTG TTGTGTGCCT GCTGAATAAC TTCTATCCCA GAGAGGCCAA TGATGACTAA ATGTTTCATA GGTTAGCTAA GAGACCTCAG GGAAGAGCGA AGAGACCTAG GCCAAGACCC TGCCTAAAGT GAGACTGGTA GTCGTCAGAC haeI mnlI တ တ dpnII[dam-] dpnI[dam+] I I K R 3901 CAGCCAGAAG ACTTCGCAAC TTATTACTGT TCACAGAGTA CTCATGTCCC GCTCACGTTT GGACAGGGTA CCAAGGTGGA 臼 asp700 (r, XmnI > Ω banI bsaJI kpnI styI csp6I asp718 DSMFI acc65I hgici cacel rsal nlaIV mbol/ndell[dam-] E v v ഗ dpnII[dam-] a bstYI/xhoII dpnI[dam+] alwi[dam-] alwI[dam-] bslIט beaWI sau3AI nlaIV bamHI maell LT asp700 bsrBI acil Iumx DSMFI ч у nlaIII bpmI/gsul[dcm-] Δ, csp6I **DSmFI** scal rsaI S bspDI[dam-] hinfI pleI a clal/bsp106 ຜ hinfi tadī U Y mboll acil A Œ II OQU bpuAI bbsI bpuAI Iloqu E D bbsI Δ,

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CITIAGACCI IGACGAAGAC AACACACGGA CGACITATIG AAGATAGGGI CICICCGGII

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TASV

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GTGGTAGACA GAAGTAGAAG GGCGGTAGAC TACTCGTCAA

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4201 CTGACGCTGA GCAAAGCAGA CTACGAGAAA CACAAAGTCT ACGCCTGCGA AGTCACCCAT CAGGGCCTGA GCTCGCCCGT CACAAAGAGC TTCAACAGG GAIGCICITI GIGITICAGA IGCGGACGCI ICAGIGGGIA GICCCGGACI CGAGCGGGCA GIGITICICG AAGIIGICCC 4101 AGTACAGTGG AAGGTGGATA ACGCCCTCCA ATCGGGTAAC TCCCAGGAGA GTGTCACAGA GCAGGACAGC AAGGACAGCA CCTACAGCCT CAGCAGCACC TICCACCIAT IGOGGGAGGI TAGCCCAITG AGGGICCICI CACAGIGICI CGICCIGICG ITCCIGICGI GGAIGICGGA GICGICGIGG fnu4HI ddeI bsoFI DbvI scfI mull aluī s L maeIII SPV hgiAI/aspHI ec113611 ddel cac8I **bsp1286** eco01091/drall **DEIHKAI** hgiJII haeIII/pall Bau96I aluI asul banili bmyI sstI Saci alwNI[dcm-] maeIII maelil hphI F > apyI[dcm+] S S ecoRII fnu4HI **betNI** cac8I bsoFI SCLFI dsav maeIII bsaJI mvaI accI H K V Y z U haeIII/palI တ sau96I O I 田 asuI bell mnli bsoFI nlaIII aluI haeIII/palI dsal sfil styl hindIII bglI ncol fnu4HI acil GACTGCGACT CGTTTCGTCT Z K A D eael blpI/bpull02I cellI/espI tru9I LTLS TCATGTCACC 34 O A hqaI csp6I rsal 151

FIG. 480

CTCTCACAAT TCGAACCGGC GGTACCGGGT TCAACAAATA ACGTCGAATA TTACCAATGT TTATTTCGTT ATCGTAGTGT TTAAAGTGTT TATTTCGTAA 4301 GAGAGIGITA AGCITGGCCG CCAIGGCCCA ACTIGITIAI IGCAGCITAI AAIGGITACA AAIAAAGCAA IAGCAICACA AAIIICACAA AIAAAGCAIT

sfaNI apol

maeIII

bbvI

bsaJI

cfrI

mseI

c o (SEQ ID NO.72)

ω

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apyI[dcm+]

betNI dsaV

ecoRII

SCLFI

mvaI

bemFI nlaIV

bsaJI



mbol/ndeII[dam-]

sau3AI

dpnII[dam-] dpnI[dam+]

pvuI/bspCI

taqI[dam-]

bsiEI mcrI

dsal haeIII/pall 4401 TITITCACIG CAITCIAGIT GIGGITIGIC CAAACICAIC AAIGIAICII AICAIGICIG GAICGAICGG GAAITAAIIC GGCGCAGCAC CAIGGCCIGA aaaaagtgac gtaagatcaa caccaaacag gtttgagtag ttacatagaa tagtacagac ctagctagcc cttaattaag ccgcgtcgtg gtaccggact haeI hhal/cfoI nlaIII bsaJI bsoFI styI ncol fnu4HI Ivqq hinPI dpnII[dam-] aseI/asnI/vspI bspDI [dam-] tru9I mseI clal/bsp106[dam-] asp700 ^sv40 mbol/ndell[dam-] dpnI[dam+] xmnI nlaIII alwI[dam-] sau3AI Hall maeI bfal DemI

TTATTGGAGA CTTTCTCCTT GAACCAATCC ATGGAAGACT CCGCCTTTCT TGGTCGACAC CTTACACACA GTCAATCCCA CACCTTTCAG GGGTCCGAGG sfani SCLFI sfaNI

4501 AATAACCTCT GAAAGAGAA CITGGTTAGG TACCTTCTGA GGCGGAAAGA ACCAGCTGTG GAATGTGTGT CAGTTAGGGT GTGGAAAGTC CCCAGGCTCC

nspBII IInad aluI

acti

mnlI ddeI

asp718 acc65I

mnlI

moll

csp6I

nlaIV

hgici kpnI banI

rsaI

nsil/avallI 4601 CCAGCAGGCA GAAGTAIGCA AAGCAIGCAI CICAAITAGI CAGCAACCAG GIGIGGAAAG ICCCCAGGCI CCCCAGCAGG CAGAAGIAIG CAAAGCAIGC nspHI cac81 Idsu ppu10I nlaIII cacel apyI[dcm+] bsmFI nlaIV ecoRII bsaJI bstNI dsav mvaI apyI[dcm+] ecoRII BCLFI dsav betNI mval sexAI nsil/avalll ppu10I nlaIII nspHI cacel sphī nspI

GGTCGTCCGT CTTCATACGT TTCGTACGTA GAGTTAATCA GTCGTTGGTC CACACCTTTC AGGGGTCCGA GGGGTCGTCC GTCTTCATAC GTTTCGTACG

cacel

OCT 2 1 2002

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES

Atty Docket: GENENT.093A

maeIII

nlalII styl

ncol

dsaI

acil bsaJI

CCGCCCCATG GCTGACTAAT

acil bsrI acil

acil

acil

DSmFI

acil fokl

TAGAGTTAAT CAGTCGTTGG TATCAGGGCG GGGATTGAGG CGGGTAGGGC GGGGATTGAG GCGGGTCAAG GCGGGTAAGA GCCGGGTAC CGACTGATTA 4701 ATCTCAATTA GTCAGCAACC ATAGTCCCGC CCCTAACTCC GCCCATCCCG CCCCTAACTC CGCCCAGTTC CGCCCATTCT

rmaI maeI bsaJI styl

avrII[dam-] haeIII/palI blnI stuI

mnll bfal haeI

ITum

start pUC118^

TITGGAGGCC TAGGCTITTG CAAAAAGCTG

bseRI

CCGAGGCCGC CTCGGCCTCT GAGCTATTCC AGAAGTAGTG AGGAGGCTTT

aluI

haeIII/palI

haeIII/pall bsaJI mnll

haeIII/palI Mnll

mnll

fnu4HI

bsoFI

bglI

sfil

AAAAAATAA ATACGTCTCC GGCTCCGGCG GAGCCGGAGA CTCGATAAGG TCTTCATCAC TCCTCCGAAA AAACCTCCGG ATCCGAAAAC GTTTTTCGAC 4801 TTTTTTTTT TATGCAGAGG

mnli bsaJi acil

hhaI/cfoI hinPI eagI/xmaIII/eclXI thaI haeIII/palI fnu4HI mcrl

fnuDII/mvnI eaeI notI

barBI bsoFI

bstul hinPI cfrI

bspMI

pstI scfI

tru9I

hhaI/cfoI cac8I ascI tru9I paci paeR7I bsiEI xhoI fnu4HI

ahaIII/draI msel tru91 bsh1236I msel msel bssHII swal mnll acil acil aval bsoFI

apyI[dcm+]

bsaJI

maell maelll

bstNI

dsav

haeIII/palI

cfrI eaeI

bsqI maeIII

ecoRII

BCLFI

mvaI

4901 TIACCICGAG CGCCGCTIA ATTAAGGCGC GCCATTIAAA TCCTGCAGGT AACAGCTIGG CACTGGCCGI CGTTTTACAA CGTCGTGACT GGGAAAACCC AATGGAGCTC GCCGGCGAAT TAATTCCGCG CGGTAAATTT AGGACGTCCA TTGTCGAACC GTGACCGGCA GCAAAATGTT GCAGCACTGA CCCTTTTGGG berI aluI sse8387I Alinearization linker inserted into Hpal site

FIG. 48Q

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mbol/ndeIl[dam-] dpnII[dam-] dpnI(dam+) pvuI/bspCI sau3AI bsiEI mcrI haeIII/palI mpli acii ear1/ksp6321 sau96I mboll cac8I asuI cac8I nspBII aluI IInad cac8I fokI fnu4HI bsoFI PPVI

fnuDII/mvnI bstUI scfI rsal hhal/cfol **bsh1236**I hinPI acil sfaNI hhal/cfol hinl1/acy1 hinPI nlaIV hgici haeII narI kası banI

ACCECAATGE GITGAATTAG CGGAACGICG IGTAGGGGGG AAGCGGTCGA CCGCATTAIC GCTTCTCCGG GCGTGGCTAG CGGGAAGGGI IGTCAACGCA

5001 TGGCGTTACC CAACTTAATC GCCTTGCAGC ACATCCCCCC TTCGCCAGCT GGCGTAATAG CGAAGAGGCC CGCACCGATC GCCCTTCCCA ACAGTTGCGT

tru9I mseI

maeIII

5101 AGCCTGAATG GCGAATGGCG CCTGATGCGG TATTTTCTCC TTACGCATCT GTGCGGTATT TCACACCGCA TACGTCAAAG CAACCATAGT ACGCGCCTG TCGGACTTAC CGCTTACCGC GGACTACGCC ATAAAAGAGG AATGCGTAGA CACGCCATAA AGTGTGGCGT ATGCAGTTTC GTTGGTATCA TGCGGGGAC bslI csp6I maell aciI acil sfaNI ahaII/bsaHI

acil fnu4HI fnu4HI bsoFI bsoFI thaI fnuDII/mvnI hinPI hinPI bstUI thaI hhaI/cfoI hinPI fnuDII/mvnI

hha1/cfoI

hinPI

bsrBI aciI

hhal/cfol haell mael

acil

bsh1236I

bstUI

hhaI/cfoI

fnu4HI bsoFI

tru9I acil

hinPI haeII

rmaI

I DOGI bfal cac81 cac8I maeIII bbvI maeIII msel bshl236I acil

FIG. 48R



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31 TITCICGCCA CETICGCCG CITICCCCGI CAAGCICIAA AICGGGGGCI CCCITIAGGG IICCGAIITA GIGCITIACG GCACCICGAC CCCAAAAAC tagI bani mnli hgici nlaIV nlaIV **bsp1286** banII bmyI aluI cfr101/bsrFI cac81

nlaIV hgiJII

hpall Idsm

maeII

AAAGAGCGGT GCAAGCGGCC GAAAGGGGGCA GTTCGAGATT TAGCCCCCGA GGGAAATCCC AAGGCTAAAT CACGAAATGC CGTGGAGCTG GGGTTTTTTG 5401 TIGATITIGG IGAIGGITCA CGIAGIGGG CAICGCCCIG AIAGACGGII ITICGCCCTI IGACGIIGGA GICCACGIIC ITIAAIAGIG GACICIIGII AACTAAACCC ACTACCAAGT GCATCACCCG GTAGCGGGAC TATCTGCCAA AAAGCGGGAA ACTGCAACCT CAGGTGCAAG AAATTATCAC CTGAGAACAA hinfI tru9I mseI hinfI maeII maell pleI haeIII/palI sau96I asuI drallI bsaAI hphI

tru9I 5501 CCAAACTGGA ACAACACTCA ACCCTATCTC GGGCTATTCT TTGATTTAT AAGGGATTTT GCCGATTTCG GCCTATTGGT TAAAAAATGA GCTGATTTAA mseI TGTTGTGAGT TGGGATAGAG CCCGATAAGA AAACTAAATA TTCCCTAAAA CGGCTAAAGC CGGATAACCA ATTTTTTACT CGACTAAATT aluI tru9I msel haeIII/palI bslI avaI bsll GGTTTGACCT

fnu4HI aciI bsoFI sfaNI alw441/snol csp61 rsaI apaLI/snoI ddeI hgiAI/aspHI bsp1286 **DSIHKAI** bmyI psp1406I maell tru9I apol tru91 msel bstUl msel fnuDII/mvnI **bsh1236I** tru9I

tru9I

sfaNI

hpall

BCLFI

fnuDII/mvnI

thal

nspBII bsh1236I

bstuI

hha1/cfo1

hinPI

ncil

Idsm

dsav fokI

GIGCACTCIC AGIACAAICI GCICIGAIGC CGCAIAGIIA AGCCAACICC gititiaaat igcgcitaaa attgititat aattgcaaat gitaaaatac cacgtgagag tcatgitaga cgagactacg gcgtatcaat tcggtfgagg mseI 5601 CAAAAATITA ACGCGAATIT TAACAAAATA ITAACGIITA CAAITITAIG mseI SSpl

hinPI fnu4HI **bsoFI**

nlaIII hhaI/cfoI bsaAI tthllll/aspI bbvI maeII bsrI

TCCCGCCATC CGCTTACAGA CGATAGCGAT GCACTGACCC AGTACCGACG CGGGGCTGTG GGCGGTTGTG GGCGACTGCG CGGGACTGCC CGAACAGACG AGGGCCGTAG GCGAATGTCT caull acil 5701 GCTATCGCTA CGTGACTGGG TCATGGCTGC GCCCCGACAC CCGCCAACAC CCGCTGACGC GCCCTGACGG GCTTGTCTGC drdI acil hgal acil

FIG. 48S

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES Hsei et al. Appl. No.: 09/234,182 Atty Docket: GENENT.093A



					mnlI	haeIII/palI	sau96I	asuI basSI	eco01091/drall	SAAAG GGCCTCGTGA	TITC CCGGAGCACT				<u> </u>
	Iu						Ilodm	PpuAI	alui bali cauli alui nlaili mnli hphi hphi bah1236i bbsi eccol091/dral	AGTATTCTTG AAGACG	STICGACACT GGCAGAGGCC CICGACGIAC ACAGICICCA AAAGIGGCAG TAGIGGCIII GCGCGCICCG ICAIAAGAAC IICIGCIIIC CCGGAGCACI	nlaIV	acil	thaI	fauDII/mvnI
thal	fnuDII/mvnI	bstol	bsh1236I	hinPI	hhaI/cfoI	thaI mnlI	fnuDII/mvnI	bstul	bsh1236I	CCCCCCAGGC	GCGCGCTCCG				
									Ihdh	ATCACCGAAA	TAGTGGCTTT				
	_								Ihqh	TITCACCGIC	AAAGTGGCAG				
									mnlI	STCAGAGGT	CAGTCTCCA				
	н			Idsu]	IHdsu	fnu4HI	bsoFI	ppvI	[aluI nlaIII	GAGCTGCATG TO	CTCGACGTAC AC				
	SCIFI	ncil	Idsm	hpall	dsaV	esp3I	bsmBI	maeIII bsmAI	bell caul	CCGTCTCCGG	SGCAGAGGCC				
								maeII	aluI	CAAGCTGTGA	GTTCGACACT				
										5801					

11111	fnuDII/mvnI	н	236I		cfoI	5901 TACGCCTATT ITTATAGGIT AAIGICAIGA TAATAAIGGT TICTTAGACG ICAGGIGGCA CITITICGGGG AAAIGIGCGC GGAACCCCTA ITTGITIATT	ATGCGGATAA AAATATCCAA TTACAGTACT ATTATTACCA AAGAATCTGC AGTCCACCGT GAAAAGCCCC TTTACACGCG CCTTGGGGAT AAACAAATAA
	fauD	bstUI	bsh1236I	hinPI	hhaI/cfoI	AAATGTGCGC (TTTACACGCG (
						CTTTTCGGG	GAAAAGCCCC
		ninlI/acyI	ahall/bsaHl	aatii	IIa	G TCAGGTGGCA	C AGTCCACCGI
		hin	aha]		ddeI maeII	r TTCTTAGAC	A AAGAATCTG
			Ħ			A TAATAATGGT	I ATTATTACCA
			nlaIII	tru9I rcaI	msel bspHI	r AATGTCATG	A TTACAGTACT
				₽	ĕ	r TTTATAGGT	A AAATATCCAA
						1 TACGCCTAT	ATGCGGATA
						590	

	mslI	TCAACATTTC AGTTGTAAAG
н	ear1/ksp6321	6001 TITCTAAATA CATTCAAATA TGTATCCGCT CATGAGACAA TAACCCTGAT AAATGCTTCA ATAATATTTGA AAAAGGAAGA GTATGAGTAT TCAACATTTC AAAGATTTAT GTAAGTTTAT ACATAGGCGA GTACTCTGTT ATTGGGACTA TTTACGAAGT TATTATAACT TTTTCCTTCT CATACTCATA AGTTGTAAAG
Ilodm	earl	AAAAGGAAG TTTTCCTTC
	Idss	ATAATATTGA TATTATAACT
		AAATGCTTCA TTTACGAAGT
		TAACCCTGAT ATTGGGACTA
bsrBI bsmAI	nlaIII	CATGAGACAA GTACTCTGTT
bsrBI	acil nlaIII	TGTATCCGCT ACATAGGCGA
		CATTCAAATA GTAAGTTTAT
		TTTCTAAATA AAAGATTTAT
		6001

rcaI bspHI

hgiAI/aspHI bsp1286	sau3AI bsiHKAI	mboI/ndeII[dam-]	dpn1[dam+] bmy1	dpnII[dam-]	eco57I apaLI/snoI	sfaNi mboli[dam-] alw441/snol
						Ihqh
						IhphI
				fnu4HI	bsoFI	acil

acil
6101 CGTGTCGCCC TTATTCCCTT TTTTGCCTTC CTGTTTTTGC TCACCCAGAA ACGCTGGTGA AAGTAAAAGA TGCTGAAGAT CAGTTGGGTG
GCACAGCGGG AATAAGGGAA AAAACGCCGT AAAACGGAAG GACAAAAACG AGTGGGTCTT TGCGACCACT TTCATTTTCT ACGACTTCTA GTCAACCCAC

NTI-IL-8 MONOCLONAL ANTIBODIES

scal hphi maelll

ddeI

fnu4HI

mcrI

acil

bsrI

csp6I rsaI

Atty Docket: GENENT.093A

mbol/ndeII[dam-]

haeIII/pall

eaeI

dpnI[dam+]



GIGCICACCC AAIGIAGCII GACCIAGAGI IGICGCCAII CIAGGAACIC ICAAAAGCGG GGCIICTIGC AAAAGGIIAC IACTCGIGAA AAITICAAGA 6201 CACGAGIGGG TIACAICGAA CIGGAICICA ACAGCGGIAA GAICCIIGAG AGIITICGCC CCGAAGAACG IITICCAAIG AIGAGCACII IIAAAGIICI ahaIII/draI bsp1286 tru91 bsiHKAI mseI hgiAI/aspHI DmyI psp1406I maelI asp700 XmnI Iloqu mbol/ndeIl[dam-] dpnII[dam-] alwI[dam-] dpn1[dam+] acil bstYI/xhoII sau3AI mbol/ndell[dam-] nspBII bsrI dpnII [dam-] alwI[dam-] bstYI/xhoII dpnI[dam+] sau3AI maeIII taqI

hpall ncil Idsm dsav eau3AI

6301 GCTATGTGGG GCGGTATTAT CCCGTGATGA CGCCGGCQAA GAGCAACTCG GTCGCCGCAT ACACTATTCT CAGAATGACT TGGTTGAGTA CTCACCAGTC CGATACACCG CGCCATAATA GGGCACTACT GCGGCCCGTT CTCGTTGAGC CAGCGGCGTA TGTGATAAGA GTCTTACTGA ACCAACTCAT GAGTGGTCAG

bcqI bsiEI bsoFI

ahaII/bsaHI

hhal/cfol

hinPI

bsh1236I

bstuI

hinll/acyI hgal cauli

fnuDII/mvnI

acil thaI dpnII [dampvul/bspCI bsiEI mcrI fnu4HI cfrI **DSOFI** acil bbvi msli nlali fnu4HI bsoFI

nlaIII

fokI

sfaNI

6401 ACAGAAAAG ATCTTACGGA TGGCATGACA GTAAGAGAAT TATGCAGTGC TGCCATAACC ATGAGTGATA ACACTGCGGC CAACTTACTT CTGACAACGA TGTCTTTTCG TAGAATGCCT ACCGTACTGT CATTCTCTTA ATACGTCACG ACGCTATTGG TACTCACTAT TGTGACGCCG GTTGAATGAA GACTGTTGCT mbol/ndeII[dam-] aluI nlaIV sau3AI mbol/ndeII[dam-] sau3AI maeIII dpnI[dam+] nlaIII sau96I avall

6501 TCGGAGGACC GAAGGAGCTA ACCGCTTTTT TGCACAACAT GGGGGATCAT GTAACTCGCC TTGATCGTTG GGAACCGGAG CTGAATGAAG CCATACCAAA AGCCTCCTGG CTTCCTCGAT TGGCGAAAAA ACGTGTTGTA CCCCCTAGTA CATTGAGCGG AACTAGCAAC CCTTGGCCTC GACTTACTTC GGTATGGTTT dpnII[dam-] bsaWI nlaili alwi[dam-] acil aluI mnll

hpaII

dpnI[dam+]

dpnII[dam-]

asuI

Hsei et al.

tru9I

mseI

ahaIII/draI

maeIII

tru9I

mseI

ban I mall

dpnII[dam-]

dpnI[dam+]

hgici

nlaIV

ddeI

sau3AI

mbol/ndeII[dam-]

tru9I mseI

opl. No.: 09/234,182 Atty Docket: GENENT.093A



asel/asnl/vspl bsmAI bsaI 6701 GACTGGATGG AGGCGGATAA AGTTGCAGGA CCACTTCTGC GCTCGGCCCT TCCGGCTGGC TGGTTATTG CTGATAAATC TGGAGCCGGT GAGCGTGGGT CTCGCGGTAT CATTGCAGCA CTGGGGCCAG ATGGTAAGCC CTCCCGTATC GTAGTTATCT ACACGACGGG GAGTCAGGCA ACTATGGATG AACGAAATAG CTGACCTACC TCCGCCTATT TCAACGTCCT GGTGAAGACG CGAGCCGGGA AGGCCGACCG ACCAAATAAC GACTATTAG ACCTCGGCCA CTCGCACCCA GAGGGCCATA GTAACGICGI GACCCCGGIC TACCATICGG GAGGCCATAG CAICAATAGA IGIGCIGCCC CICAGICCGI IGAIACCIAC IIGCITIAIC 6601 CGACGAGCGT GACACCACGA TGCCAGCAGC AATGGCAACA ACGTTGCGCA AACTATTAAC TGGCGAACTA CTTACTCTAG CTTCCGGGA ACAATTAATA GCTGCTCGCA CIGIGGIGCI ACGGICGICG TIACCGIIGI IGCAACGCGI TIGAIAAITG ACCGCIIGAI GAAIGAGAIC GAAGGGCCGI IGIIAAITAI tru91 mseI cfr101/bsrFI bpmI/gsuI[dcm-] nlaIV hphI hpall Idsm fokI hpall Idsw SCLFI dsaV cauII ncil aluI rmal maeI bfaI ahdi/eam1105i hinfI berI tru9I mseI cac8I hpall Idsm haeIII/palI hhal/cfol avill/fspI sau96I hinPI bglI mstI asuI psp1406I hhaI/cfoI maeI] hinPI mnlI haeIII/palI cac8I bsrDI sau96I avall asuI fnu4HI **bsoFI** sfani bbvi sau96I nlaIV berI asuI fnu4HI bsoFI bbvI acil mslI bsh1236I bsrDI maelli fnuDII/mvnI mnlI fokI acil bstul thaI 6801

mbol/ndeII[dam-] dpnII[dam-] dpnI[dam+] sau3AI TITAAAAGGA TCTAGGTGAA GATCCTTTTT GATAATCTCA TGACCAAAAT CCCTTAACGT GAGTTTTCGT TCCACTGAGC GTCAGACCCC GTAGAAAGA 6901 ACAGATCGCT GAGATAGGTG CCTCACTGAT TAAGCATTGG TAACTGTCAG ACCAAGTTTA CTCATATATA CTTTAGATTG ATTTAAAACT TCATTTTAAA TGTCTAGGGA CTCTATCCAC GGAGTGACTA ATTCGTAACC ATTGACAGTC TGGTTCAAAT GAGTATATAT GAAATCTAAC TAAATTTTGA AGTAAAATT ddeI maeII tru9I mseI nlallI bspHI rcal mbol/ndeII[dam-] dpnII[damdpnI[dam+] alwI[dam-] bstYI/xhoII ahaiii/drai bfai mboii[dam-] sau3AI mbol/ndeII[dam-] sau3AI hphI dpnII[dam-] tru9I betYI/xhoII dpnI[dam+] alwI[dam-] maeI rmaI 7001

CTCAAAAGCA AGGTGACTCG CAGTCTGGGG CATCTTTTCT AAATTITCCI AGAICCACII CIAGGAAAAA CIAITAGAGI ACIGGIIITA GGGAATIGCA



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mbol/ndell[dam-] sau3AI

dpnII[dam-] dpnI[dam+]

alwi[dam-] mspl

hpall

acil

cac8I

fnuDII/mvnI

mbol/ndell[dam-] thal

sau3AI

mboll[dam-]

fnu4HI

bsh1236I

dpnII[dam-] dpnII[dam-]

bstul

dpnI[dam+]

dpnI[dam+]

mbol/ndeII[dam-]

bsoFI bbvI

hinPI

alwI[dam-] bstYI/xhoII

bstYI/xhoII alwI[dam-]

hhaI/cfoI

7101 TCAAAGGATC TTCTTGAGAT CCTTTTTTTC

acil

aluI

GTTTGTTTGC CGGATCAAGA TGCGCGTAAT CTGCTGCTTG CAAACAAAA AACCACCGCT ACCAGCGGTG nspBII

AGTITCCTAG AAGAACTCTA GGAAAAAAG ACGCGCATTA GACGACGAAC GTITGTITI ITGGTGGCGA TGGTC3CCAC CAAACAAACG GCCTAGTTCT

haeIII/palI maeI rmaI

7201 GCTACCAACT CITITICCGA AGGTAACTGG CITCAGCAGA GCGCAGATAC CAAATACTGT CCTTCTAGTG TAGCCGTAGT TAGGCCACCA CTTCAAGAAC CGATGETTGA GAAAAAGGCT TCCATTGACC GAAGTCGTCT CGCGTCTATG GTTTATGACA GGAAGATCAC ATCGGCATCA ATCCGGTGGT GAAGTTCTTG haeI bslI bfaI

hhal/cfol

eco57I

bsrI maelll

hinPI

ncil Idem fnu4HI **DBOFI** DbvI

fnu4HI alwNI[dcm-]

bsrI bsrI bsoFI

7301 TCTGTAGCAC CGCCTACATA CCTCGCTCTG CTAATCCTGT TACCAGTGGC TGCTGCCAGT GGCGATAAGT CGTGTCTTAC CGGGTTGGAC TCAAGACGAT bbvI maeIII

mnlI

acil

hinfi pleI

cauli

hpall dsav AGACATCGTG GCGGATGTAT GGAGCGAGAC GATTAGGACA ATGGTCACCG ACGACGGTCA CCGCTATTCA GCACAGAATG GCCCAACCTG AGTTCTGCTA

hgiAI/aspHI **bsp1286 DSIHKAI**

apaLI/snoI bmyI

alw44I/snoI

hinPI bsiEI

bbvI mcrI

hpall bsaWI

maelil

Idsm

nspBII

Enu4HI **bsoFI** aluI

scfI

ddeI

ITCGTGCACA CAGCCCAGCT TGGAGCGAAC GACCTACACC GAACTGAGAT ACCTACAGCG 7401 AGTTACCGGA TAAGGCGCAG CGGTCGGGCT GAACGGGGGG TTCGTGCACA CAGCCCAGCT TGGAGCGAAC GACCTACACC GAACTGAGAT ACCTACAGC TCAATGGCCT ATTCCGCGTC GCCAGCCCGA CTTGCCCCCC AAGCACGTGT GTCGGGTCGA ACCTCGCTTG CTGGATGTGG CTTGACTCTA TGGATGTCGC hhal/cfol

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scrF] mvaI

aluI apyI[dcm+] ecoRII betNI dsav bsaJI 7501 TGAGCATTGA GAAAGCGCCA CGCTTCCCGA AGGGAGAAAG GCGGACAGGT ATCCGGTAAG CGGCAGGGTC GGAACAGGAG AGCGCACGAG GGAGCTTCCA ACTCGTAACT CITICGCGGI GCGAAGGGCI ICCCICITIC CGCCIGICCA TAGGCCAIIC GCCGICCCAG CCITGICCTC ICGCGIGCIC CCICGAAGGI CCIGGIAICI TIAIAGICCI GICGGGIITC GCCACCICIG ACTIGAGCGI CGAITITIGI GAIGCICGIC AGGGGGGGGG AGCCIAIGGA CCCCTTTGC GGACCATAGA AATATCAGGA CAGCCCAAAG CGGTGGAGAC TGAACTCGCA GCTAAAAACA CTACGAGCAG TCCCCCCGCC TCGGATACCT nlaIV hinPI mnll hhaI/cfoI bssSI fnu4HI **bsoFI** acil tagI nspHI haeIII/pall nspI hgaI nlallI hpall bell bsaWI mnli drdi haeI haeIII/palI apyI[dcm+] mval bsll ecoRII SCLFI bstNI dsaV haeIII/palI fnuDII/mvnI hhal/cfol thal bslI apy1[dcm+] fnu4HI hinPI bsoFI haeII acil bstul ecoRII SCIFI bstNI mvaI dsav 7601 GGGGGAAACG

FIG. 48X

7801 TATTACCGCC TITGAGTGAG CTGATACCGC TCGCCGCAGC CGAACGACCG AGCGCAGCGA GTCAGTGAGC GAGGAAGCGG AAGAGCGCC AATACGCAAA ATAATGGCGG AAACTCACTC GACTATGGCG AGCGGCGTCG GCTTGCTGGC TCGCGTCGCT CAGTCACTCG CTCCTTCGCC TTCTCGCGGG TTATGCGTTT

mboll hhal/cfol

sapI hinPI

earI/ksp632I

haeII

acil

mnll

bbvI pleI hinPI hinfI

fnu4HI

fnu4HI

bsoFI bbvI

bsoFI

hhaI/cfoI

bsiEI

ncrI

bsrBI fnu4HI

bsoFI

acil

aluI

cac8I acil

7701 AAAACGCCAG CAACGCGGCC TTTTTACGGT TCCTGGCCTT TTGCTGGCCT TTTGCTCACA TGTTCTTTCC TGCGTTATCC CCTGATTCTG TGGATAACCG TTTTGCGGTC GTTGCGCCGG AAAAATGCCA AGGACCGGAA AACGACCGGA AAACGAGTGT ACAAGAAAGG ACGCAATAGG GGACTAAGAC ACCTATTGGC

cac8I

nlaIV haeI

bsh12361

cac8I

aflIII

hinfi



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maeIII asel/asnl/vspl 7901 CCGCCTCTCC CCGCGCGTTG GCCGATTCAT TAATCCAGCT GGCACGACAG GTTTCCCGAC TGGAAAGCGG GCAGTGAGCG CAACGCAATT AATGTGAGTT GGCGGAGAGG GGCGCGCAAC CGGCTAAGTA ATTAGGTCGA CCGTGCTGTC CAAAGGGCTG ACCTTTCGCC CGTCACTCGC GTTGCGTTAA TTACACTCAA mseI hhaI/cfoI hinPI cacel acil bsrI cac81 eael tfil asel/asnl/vspl aluI nspBII IInad hinfI mseI tru9I haelll/pall fnuDII/mvnI cfrI fnuDII/mvnI **bsh1236**I hhal/cfol bsh1236I bstUI bstul hinPI thaI acil bslI mnll

FIG. 48Y

8001 ACCICACICA TIAGGCACCC CAGGCITIAC ACTITATGCI TCCGGCTCGI ATGITGTGG GAATIGTGAG CGGATAACAA TITCACACAG GAAACAGCTA TGGAGTGAGT AATCCGTGGG GTCCGAAATG TGAAATACGA AGGCCGAGCA TACAACACAC CTTAACACTC GCCTATTGTT AAAGTGTGTC CTTTGTCGAT

hpall

hgicI apyI[dcm+]

banI bsaJI

mnlI

nlaIV bstNI

ecoRII

mvaI

dsav

SCIFI

acil bsrBI

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tru9I

alw441/snoI(GTGCAC):



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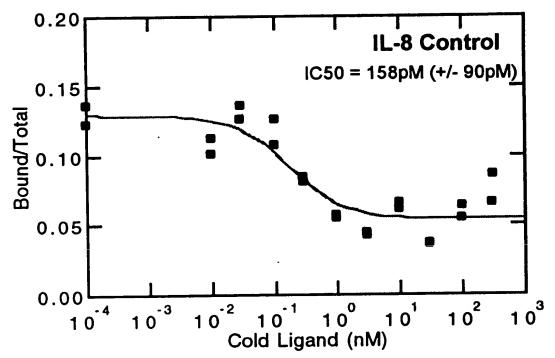


FIG. 49A

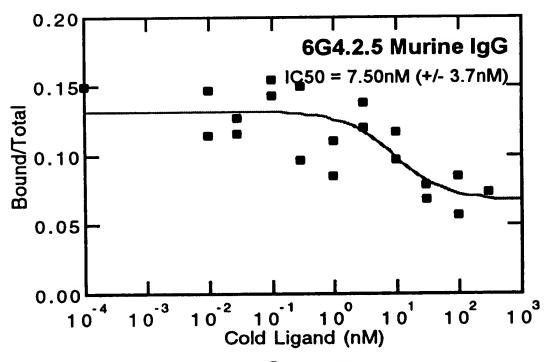


FIG. 49B

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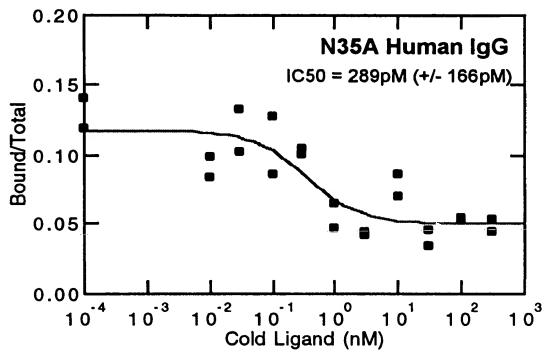


FIG. 49C

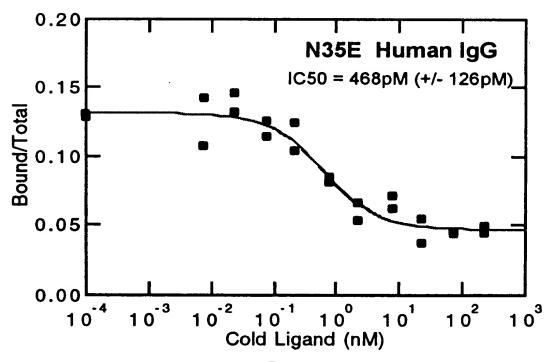
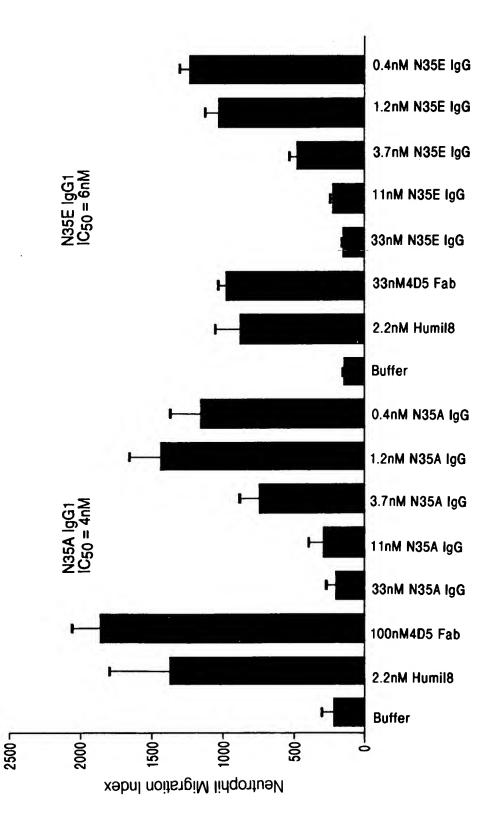


FIG. 49D

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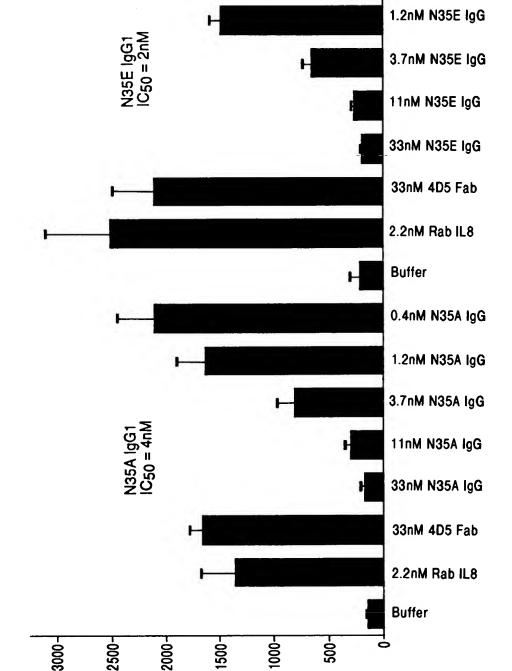
3000

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0.4nM N35E lgG

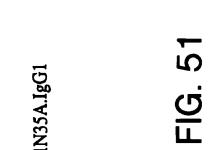


Meutrophil Migration Index

FIG. 50B



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88pM

7.7x10⁻⁵

 $8.7x10^{5}$

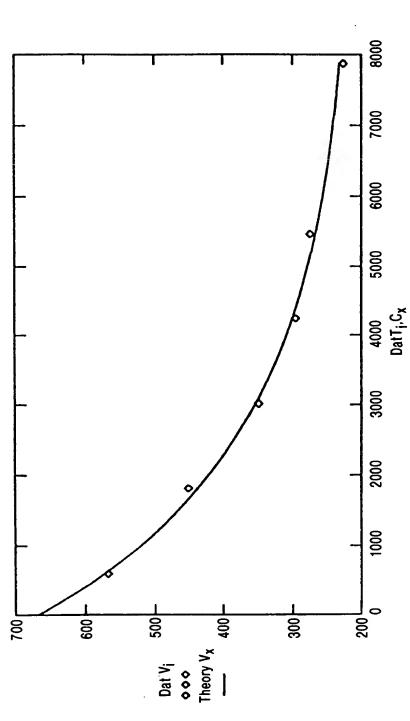
6G4V11N35A-IgG1

49pM

 $1.4x10^{-4}$

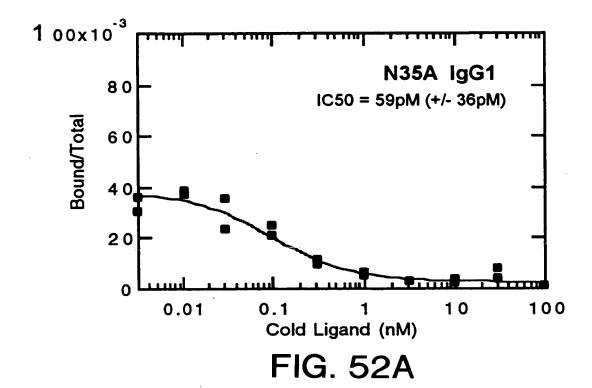
 3.0×10^6

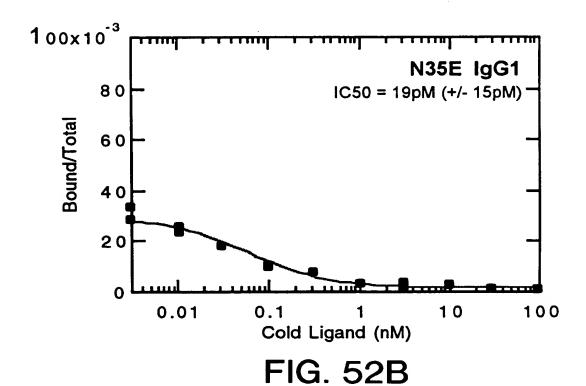
6G4V11N35E-IgG1



Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.IgG1 350pM 2.9x10-4 kd 8.3×10^{5} Ka Murine 6G4.2.5 IgG2a SAMPLE

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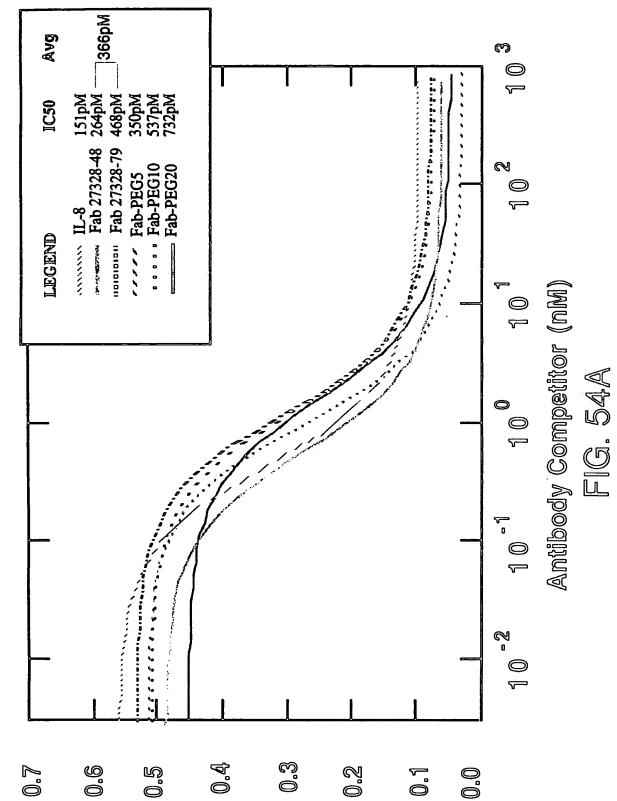
781 -1	AAAAGGGTAT TTTTCCCATA	CTAGAGGTTG GATCTCCAAC	AGGTGATTTT TCCACTAAAA	TACTTTTTCT	ATATCGCATT TATAGCGTAA I A F	AGAAGAACGT
_		ТТТТТСТАТ	macmacaaac	CCCMACCCMC	እርርመመር እርርጥ	እርጥኖር እርጥኖጥ
	AGATACAAGC	AAAAAAGATA	ACGATGTTTG	CGCATGCGAC	TCCAAGTCGA	TCACGTCAGA
-11	S M F V	F S I	ATN	AYAE	V Q L	v Q s
901	GGCGGTGGCC	TGGTGCAGCC ACCACGTCGG	AGGGGGCTCA	CTCCGTTTGT	CCTGTGCAGC	TTCTGGCTAC
8		V Q P				
961		GTCACTATAT				
		CAGTGATATA				
28	S F S S	<u>нум</u>	_H w v	RQAP	GKG	LEW
1021	GTTGGATATA	TTGATCCTTC AACTAGGAAG	CAATGGTGAA	ACTACGTATA	ATCAAAAGTT	CAAGGGCCGT
48		D P S				
	-					
1081		CTCGCGACAA GAGCGCTGTT				
68		R D N				
1141	GCTGAGGACA	CTGCCGTCTA GACGGCAGAT	TTACTGTGCA	AGAGGGGATT	ATCGCTACAA	TGGTGACTGG
88		A V Y				
	•					
1201		TCTGGGGTCA				
100		AGACCCCAGT W G Q				
100_	F F D V	W G Q	G 1 L			
1261		TCCCCCTGGC				
100		AGGGGGACCG P L A				
128	PSVF	РЬА	PSS	K 5 1 5	G G I	A A D
1321		TCAAGGACTA				
		AGTTCCTGAT				
148	GCLV	K D Y	F P E	PVTV	SWN	S G A
1381		GCGTGCACAC				
168		CGCACGTGTG V H T				
				_		
1441		TGACCGTGCC ACTGGCACGG				
188		T V P				
1501		CCAGCAACAC GGTCGTTGTG				
208		S N T				
1561		GCCCGCCGTG/ CGGGCGCAC		9)		
228		P P O		0)		
	•		(•		

FIG. 53

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ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES

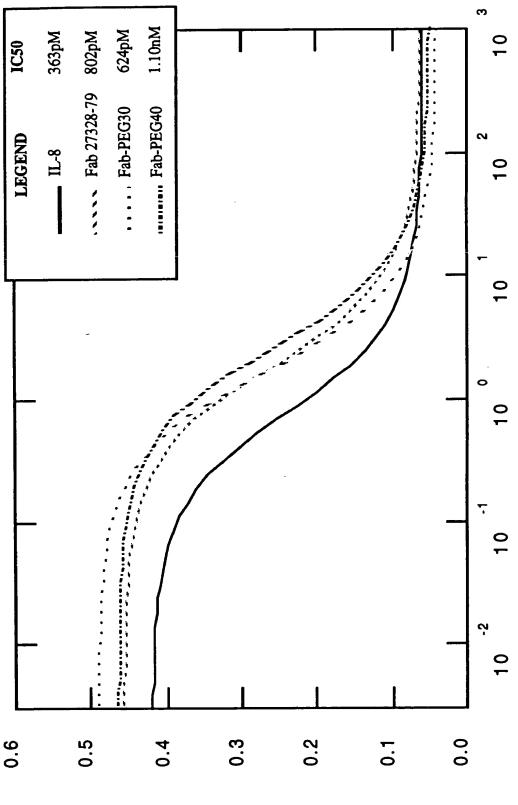
Hsei et al.





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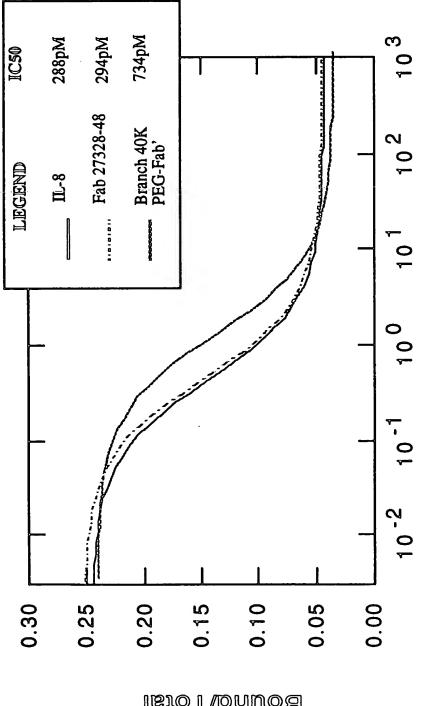
Bound/Total

Antibody Competitor (nM) FIG. 54B



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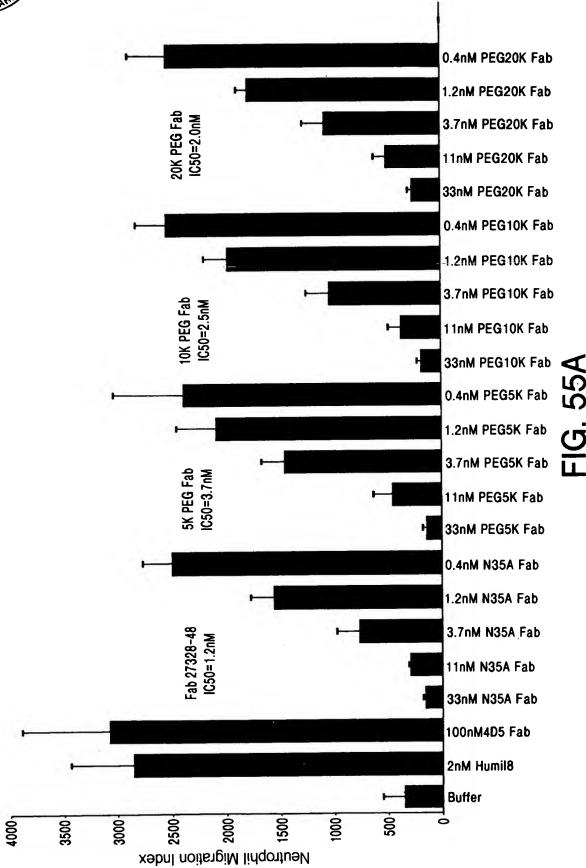


Antibody Competitor (nM)

1stoT\bnuo8



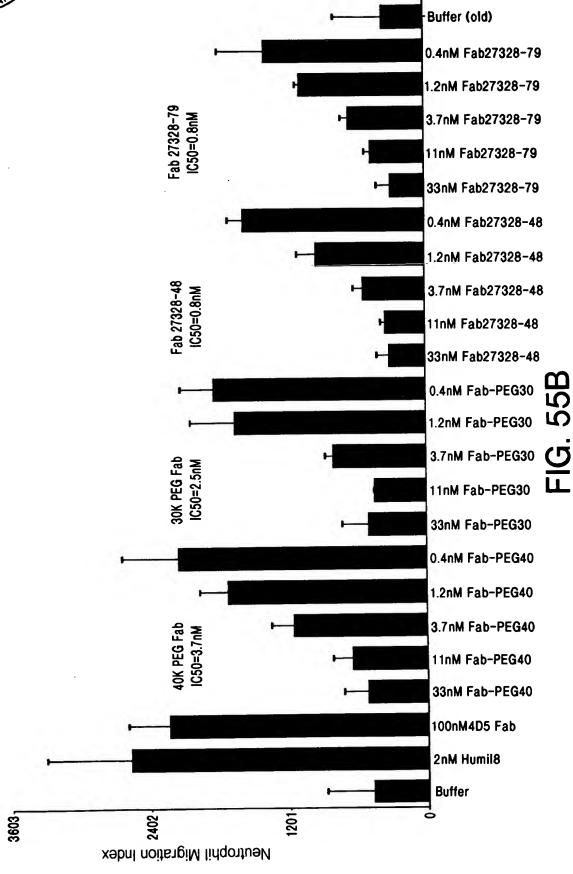
Hsei et al.



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ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.



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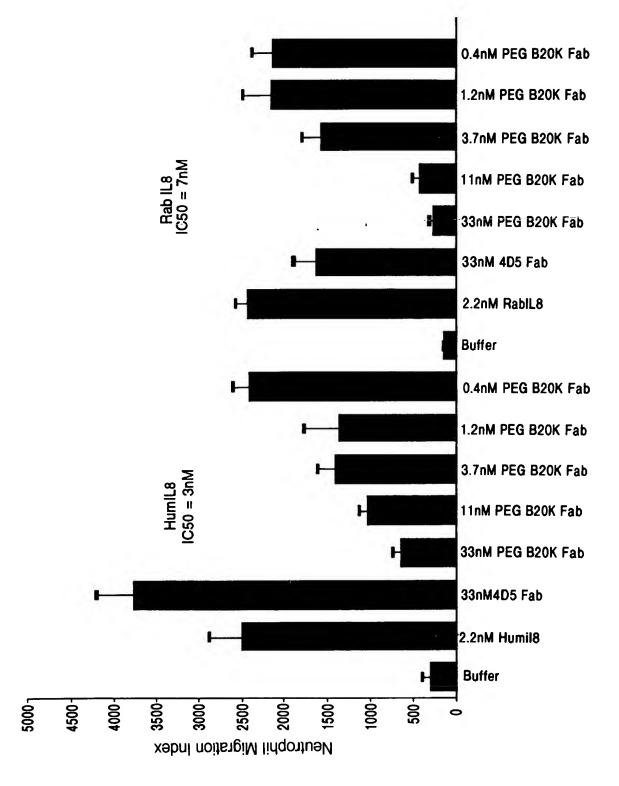
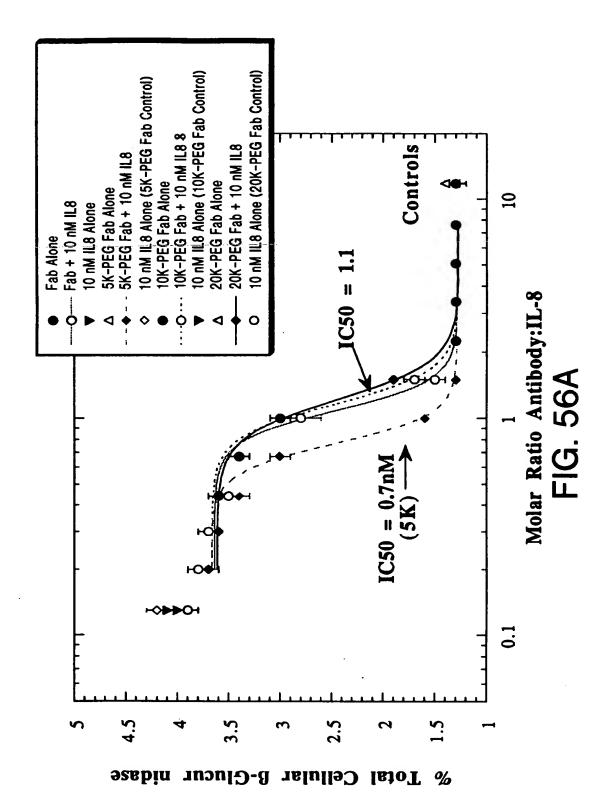


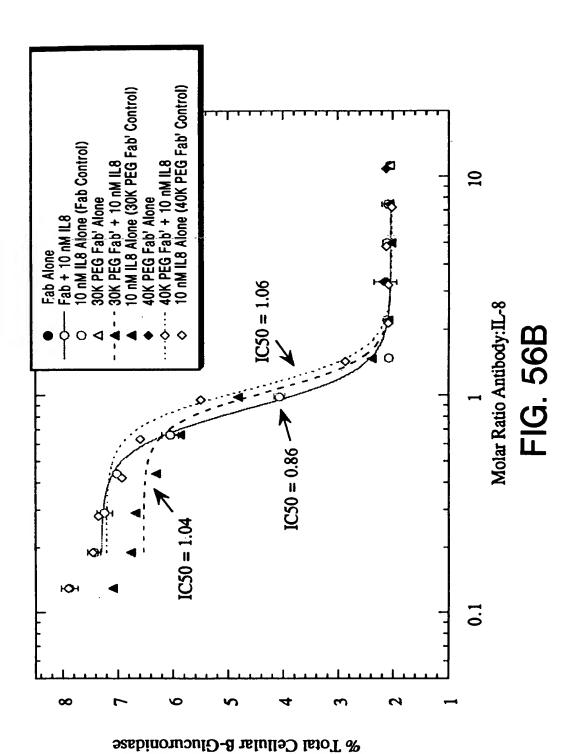
FIG. 55C



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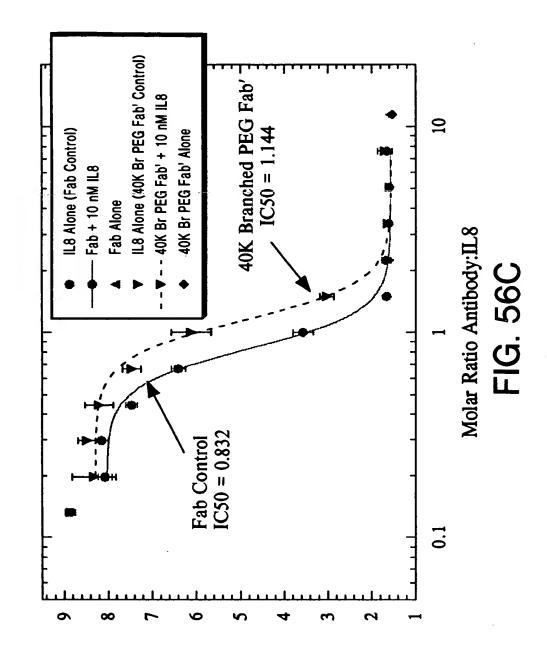






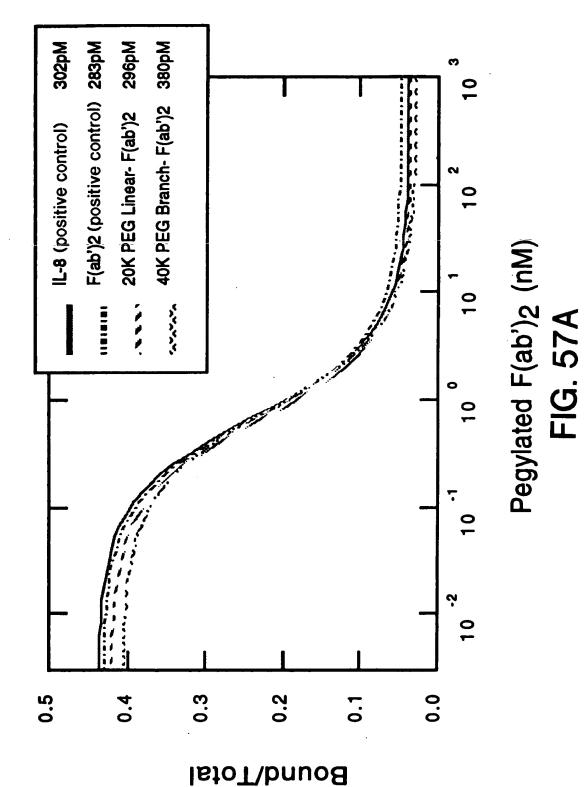
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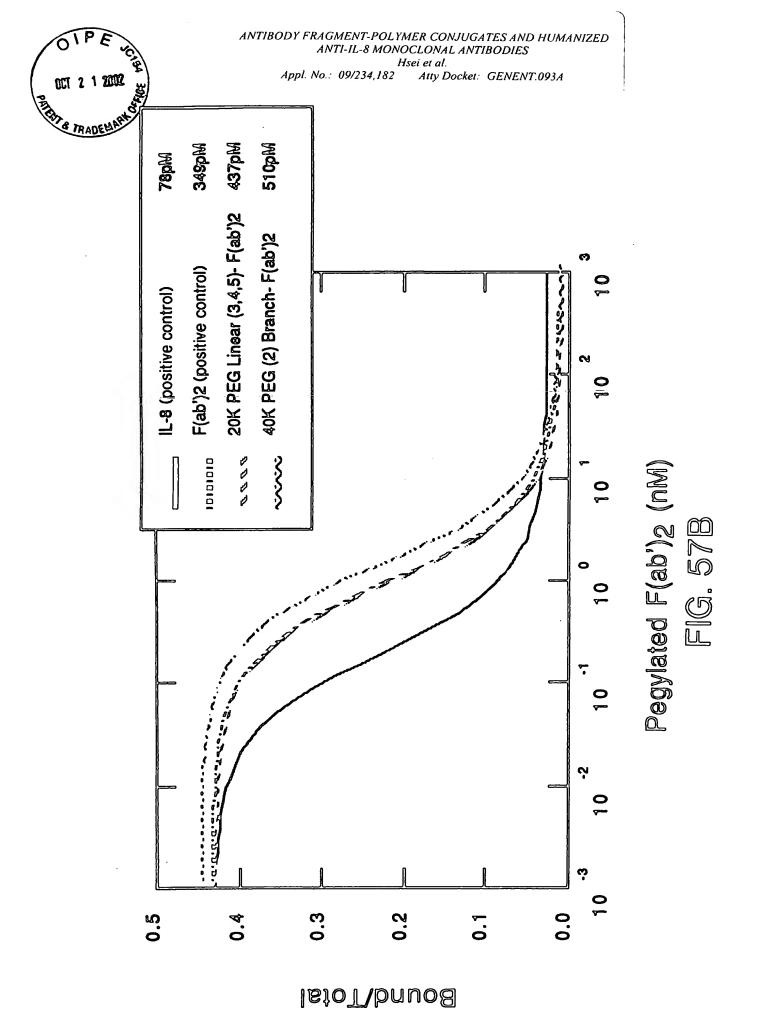


% Total Cellular B-Glucuronidase Activity



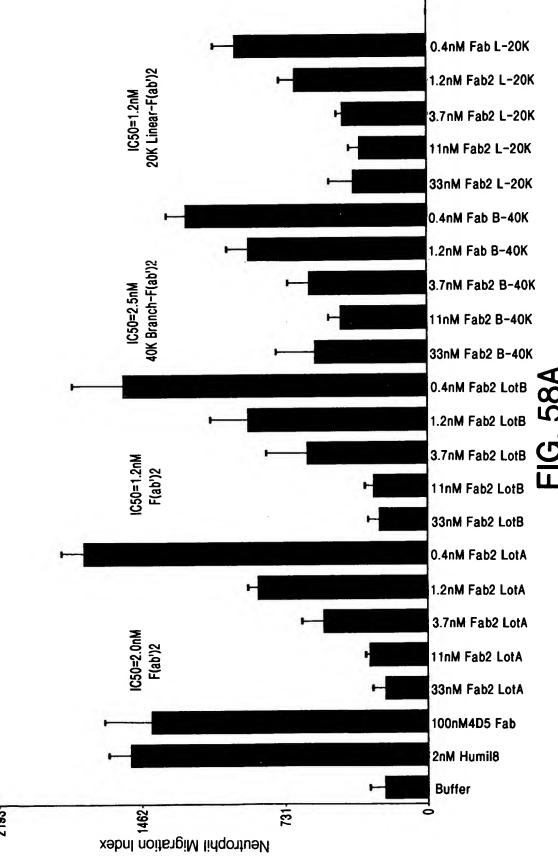


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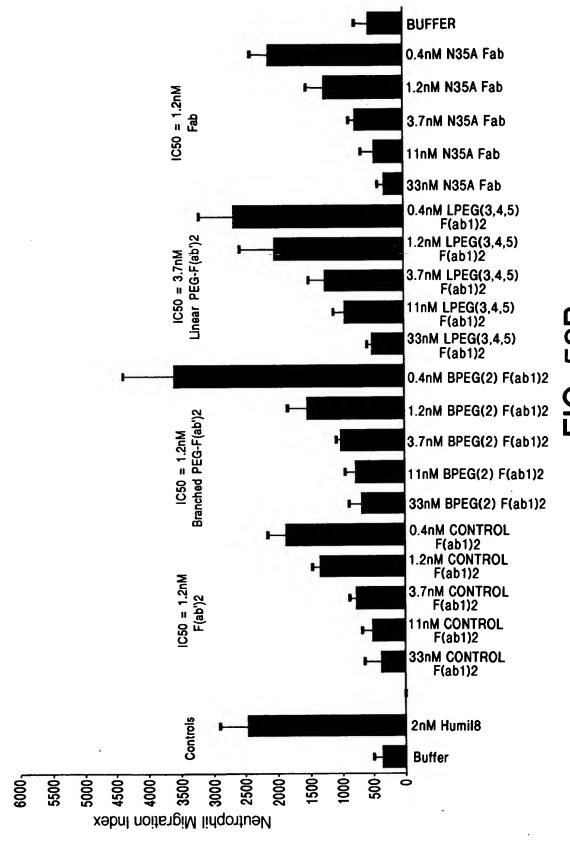




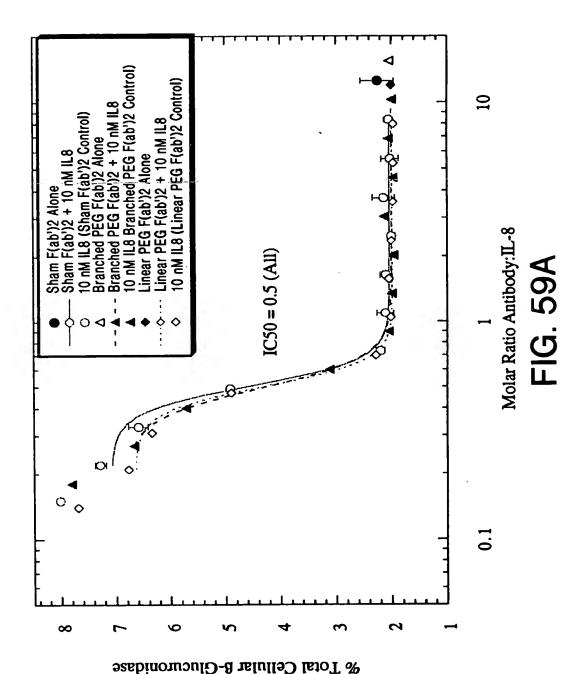
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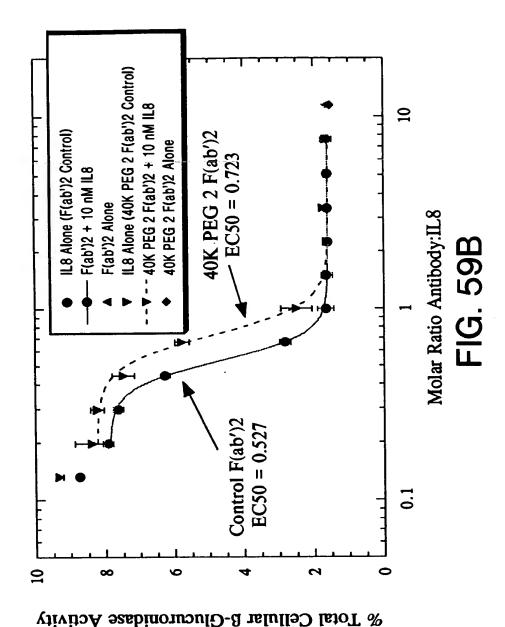






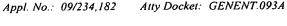


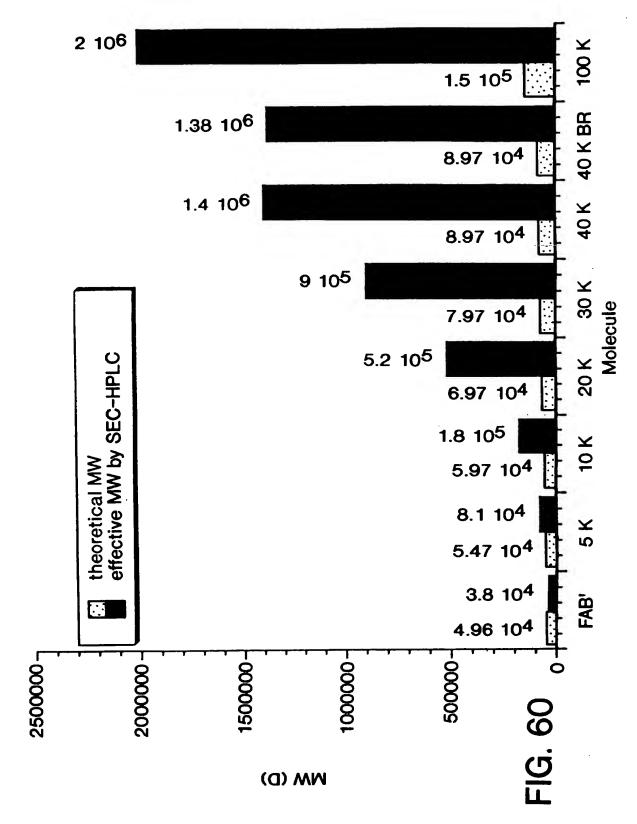






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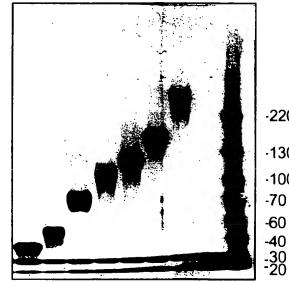


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Reduced



-220

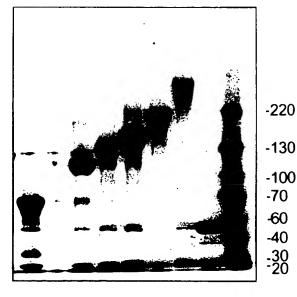
-130

-100 -70 -60

FIG. 61A

-20K -30K -40K -40K branch 100K

Non-Reduced



Fab-PEG-5000

FIG. 61B

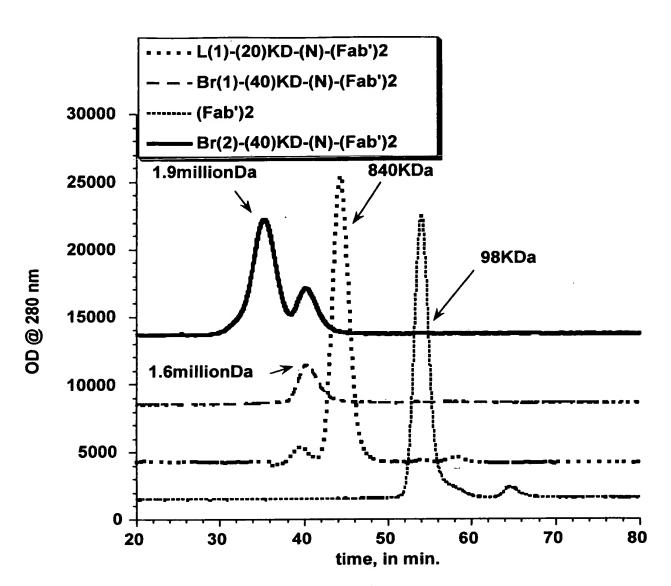


FIG. 62





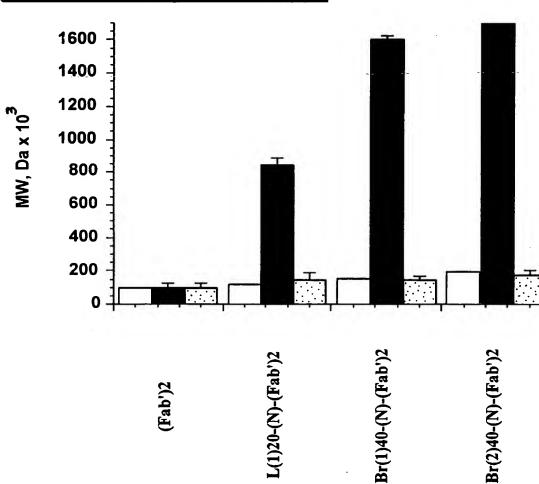


FIG. 63



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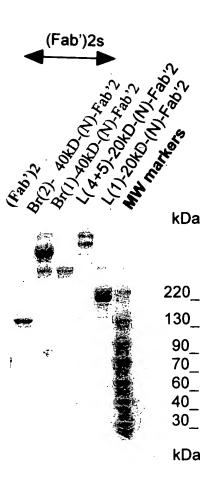
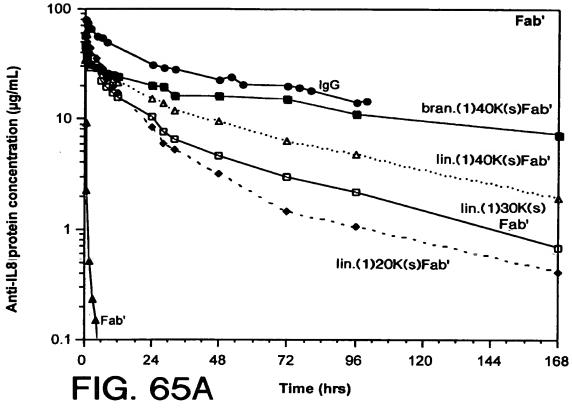
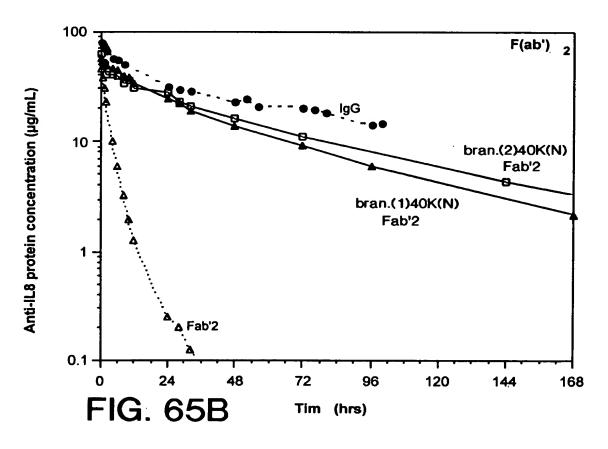


FIG. 64



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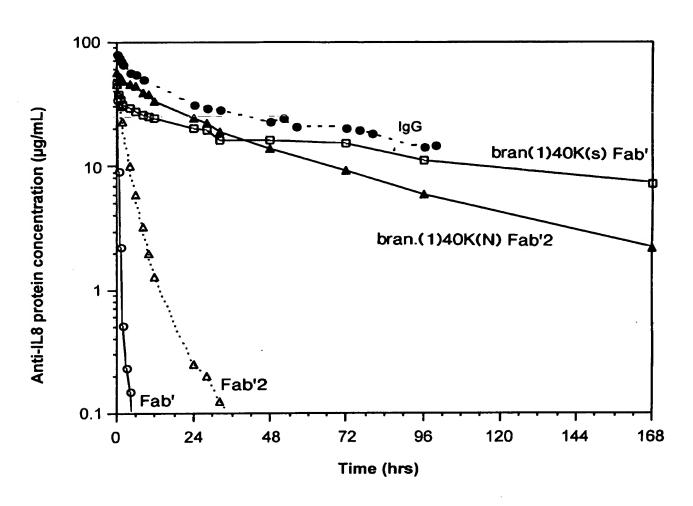
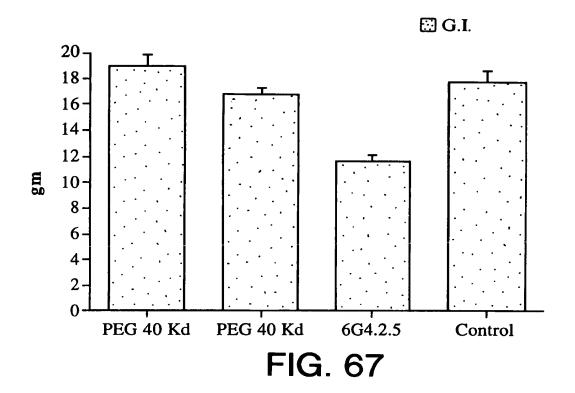
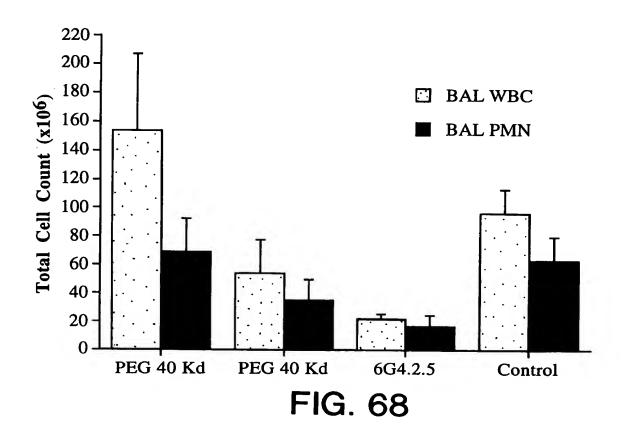


FIG. 66



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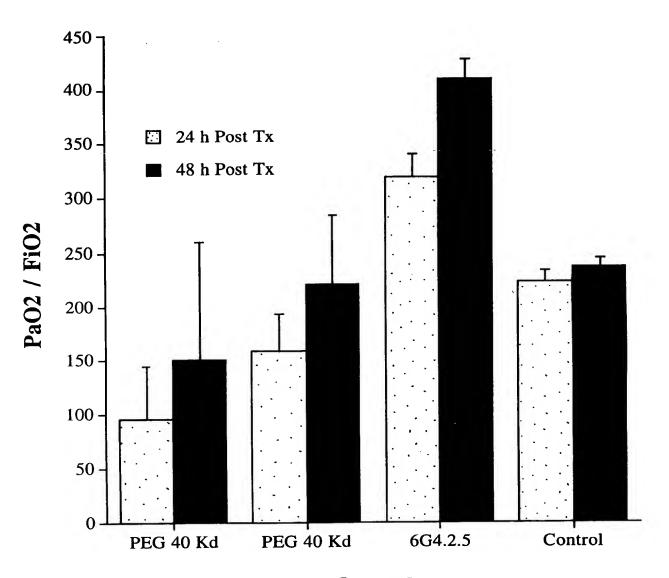


FIG. 69



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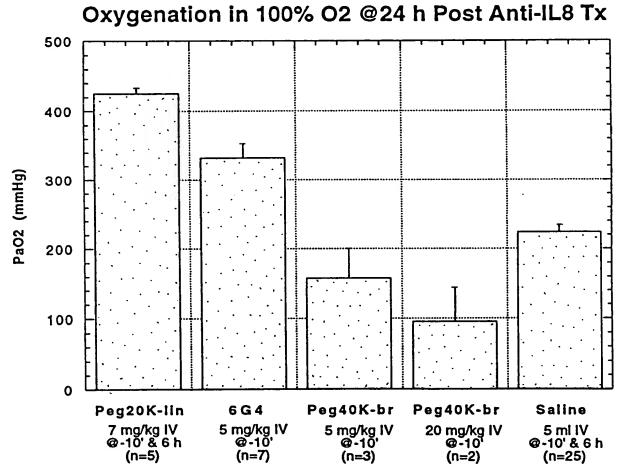


FIG. 70A



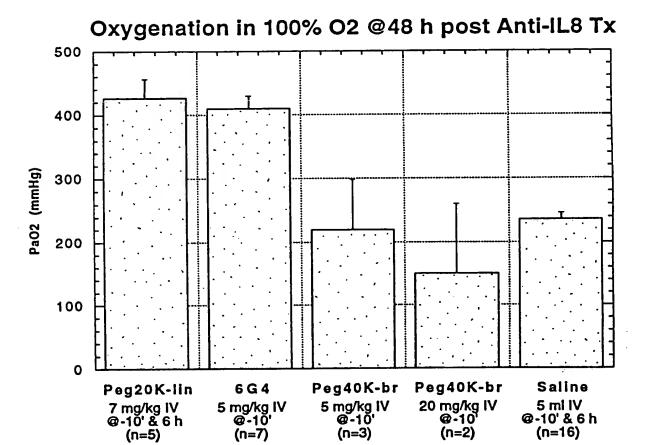


FIG. 70B



GLW / BW Ratio

Peg20K-lin

7 mg/kg IV @-10' & 6 h

(n=5)

6 G 4

5 mg/kg IV @-10'

(n=7)

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Gross Lung Weight to Body Weight Ratio

FIG. 70C

Peg40K-br

5 mg/kg IV @-10'

(n=3)

Peg40K-br

20 mg/kg IV @-10

(n=3)

Saline

5 ml IV @-10' & 6 h (n=29)



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Total WBC in BAL Fluid

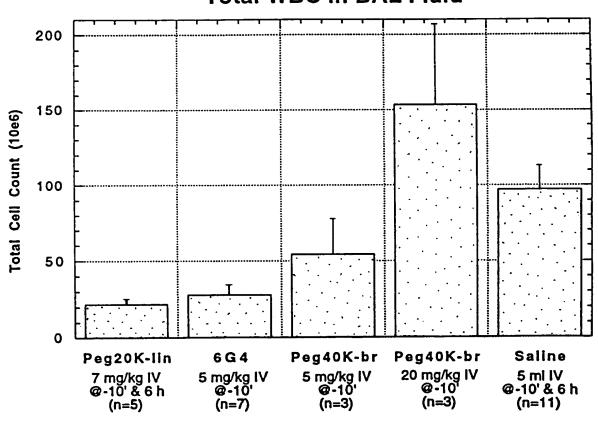


FIG. 70D



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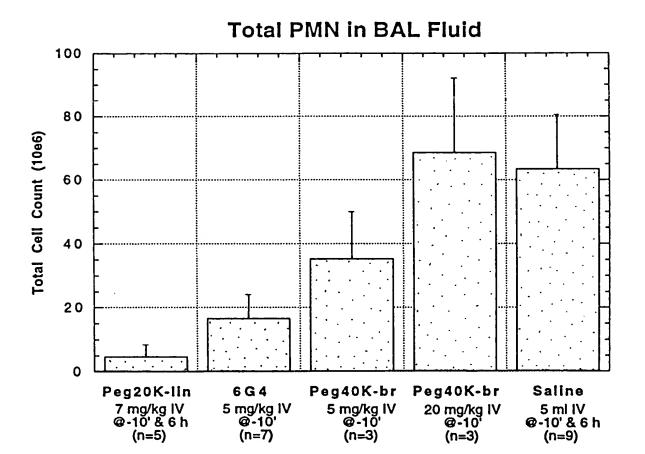
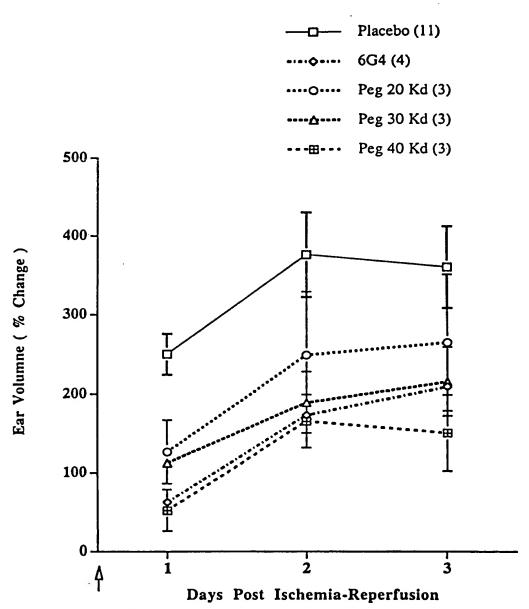


FIG. 70E



Appl. No.: 09/234,182 Atty Docket: GENENT.093A

The Effect of Pegylated Anti-IL-8 in the Rabbit Ear model of Ischemia-Reperfusion Injury



Anti-IL-8 formulations: Single Dose (5 mg/kg) administered IV at time of reperfusion

FIG. 71